Washington State Health Care Authority

Tinnitus: Non-invasive, Non-pharmacologic Treatments

Draft Evidence Report

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Health Technology Assessment Program (HTA)

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The information in this report is intended to help the State of Washington's independent Health Technology Clinical Committee make well-informed coverage determinations. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information (i.e., in the context of available resources and circumstances presented by individual patients).

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Contents

Contents i
List of Appendices ii
List of Figures ii
List of Tables ii
List of Abbreviations iv

Executive Summary ES-1
Structured Abstract ES-1
ES 1. Background ES-2
ES 2. Methods ES-3
ES 3. Results ES-6
ES 4. Discussion ES-9
ES 5. Conclusion ES-11

Full Technical Report 1
1. Background 1
1.1 Condition Description 1
1.2 Disease Burden 1
1.3 Technology Description 2
1.4 Regulatory Status 4
1.5 Policy Context 4
1.6 Washington State Agency Utilization Data 4
2. Methods 4
2.1 Research Questions and Analytic Framework 5
2.2 Data Sources and Searches 6
2.3 Study Selection 6
2.4 Data Abstraction and Risk of Bias Assessment 9
2.5 Data Synthesis and Quality of Evidence Rating 9
3. Results 10
3.1 Overview of Outcomes Used and Analyses Reported 12
3.2 Sound Therapy Interventions 19
3.3 Repetitive Transcranial Magnetic Stimulation Interventions 26
3.4 Cognitive Behavioral Therapy Interventions 32
3.5 Tinnitus-Specific Interventions 41
4. Discussion 49
4.1 Summary of the Evidence 49
4.2 Limitations of the Evidence Base 51
4.3 Clinical Practice Guidelines and Related Health Technology Assessments 51
4.4 Selected Payer Coverage Policies 53
4.5 Limitations of This HTA 56
4.6 Ongoing Research 56

Conclusion 57
5. References 58

List of Appendices

Appendix A. State of Washington Health Care Authority Utilization Data A-1
Appendix B. Additional Background B-1
Appendix C. Search Strategy C-1
Appendix D. Evidence Tables D-1
Appendix E. Excluded Articles E-1
Appendix F. Individual Study Risk of Bias Assessments F-1
Appendix G. Studies Using Comparative Effectiveness, Neuromodulation, or Psychological Therapies Outside the Scope of This Review G-1
Appendix H. Detailed GRADE Assessments H-1
Appendix I. Agree-II Clinical Practice Guideline Ratings I-1
Appendix J. Additional Information About Ongoing Studies J-1

List of Figures

Figure ES-1. Analytic framework for Health Technology Assessment on Non-pharmacologic, Non-invasive Treatments for Tinnitus ES-4
Figure 1. Analytic framework for Health Technology Assessment on Non-pharmacologic, Non-invasive Treatments for Tinnitus 5
Figure 2. Study Flow Diagram for HTA on Non-invasive, Non-pharmacologic Treatments for Tinnitus 11

List of Tables

Table ES-1. Summary of GRADE Certainty Ratings for Non-invasive, Non-pharmacologic Interventions for Tinnitus Included in This HTA ES-9
Table ES-2. Overview of Payer Coverage Policies for Tinnitus ES-11
Table 1. Population, Intervention, Comparator, Outcomes, Timing, Setting and Other Study-Selection Criteria for HTA on Non-invasive, Non-pharmacological Treatment of Tinnitus 6
Table 2. Certainty of Evidence Grades and Definitions[43] 10
Table 3. Summary of Validated Tinnitus Distress and Disability Measures Reported by Included Studies. 13
Table 4. Summary of Validated Measures of Psychological Status and Quality of Life Reported by Included Studies. 15
Table 5. Summary of Study Characteristics of Included Studies of Sound Therapies for the Treatment of Tinnitus 21
Table 6. Summary of Study Characteristics of Included Studies of Repetitive Transcranial Magnetic Stimulation for the Treatment of Tinnitus 28
Table 7. Summary of Study Characteristics of Included Studies of Cognitive Behavioral Therapy for the Treatment of Tinnitus 35
Table 8. Summary of Study Characteristics of Included Studies of Tinnitus-specific Interventions for the Treatment of Tinnitus 43
Table 9. Summary of GRADE Certainty Ratings for Non-invasive, Non-pharmacologic Interventions for Tinnitus Included in This HTA 49
Table 10. Summary of Clinical Practice Guidelines for the Treatment of Tinnitus 52
Table 11. Overview of Payer Coverage Policies for Tinnitus 53

Table 12. Detailed Payer Coverage Policies for Tinnitus.....54
Table 13. Relevant Clinical Trials by Status and Intervention Category.....56

List of Abbreviations

ADS	Allgemeine Depression Scale
AMD	Absolute mean difference
BDI	Beck Depression Inventory
CBT	Cognitive behavioral therapy
CGI	Clinical Global Improvement Scale
CI	Confidence interval
COPE	Coping Inventory
CPG	Clinical practice guidelines
DASS	Depression and Anxiety and Stress Scale
DSP	Derogatis Stress Profile
ES	Executive summary
ESS	Epworth Sleepiness Scale
GHQ-12	General Health Questionnaire-12 items
HADS	Hospital Anxiety and Depression Scale
HAM-A	Hamilton Anxiety Rating Scale
HAM-D	Hamilton Depression Rating Scale
HTA	Health technology assessment
ISI	Insomnia Severity Index
JSEQ	Jenkins Sleep Evaluation Questionnaire
NR	Not reported
NS	Not significant
PSQ	Perceived Stress Questionnaire
PSS	Perceived Stress Scale
QoL	Quality of life
QoLI	Quality of Life Inventory
RD	Risk difference
RR	Risk ratio
SCL-90R	Symptom Checklist 90-Revised
SF-12,36	Short Form Survey (36 or 12 item)
TAQ	Tinnitus Acceptance Questionnaire
TCQ	Tinnitus Cognitions Questionnaire
TCSQ	Tinnitus Coping Style Questionnaire
TDQ	Tinnitus Disability Questionnaire

TEfQ	Tinnitus Effects Questionnaire
TExQ	Tinnitus Experience Questionnaire
TFI	Tinnitus Functional Index
THI	Tinnitus Handicap Inventory
THQ	Tinnitus Handicap Questionnaire
TQ	Tinnitus Questionnaire
TRFI	Tinnitus-related Fear Index
TRQ	Tinnitus Reaction Questionnaire
TSI	Tinnitus Severity Index
TSS	Tinnitus Severity Scale
U.K.	United Kingdom
U.S.	United States
VAS	Visual analog scale
WCCL-R	Ways of Coping Checklist Revised
WHO QOL	World Health Organization Quality of Life

Executive Summary

Structured Abstract

Purpose: To conduct a health technology assessment (HTA) on the efficacy, safety, and cost of non-invasive, non-pharmacological treatments for tinnitus.

Data Sources: PubMed, Embase, PsycINFO, Cochrane Library from inception through September 9, 2019; clinical trial registry; government, payor, and clinical specialty organization websites; hand searches of systematic reviews.

Study Selection: Using a priori criteria, we selected English-language primary research studies that were conducted in very highly developed countries that reported effectiveness, safety, or cost outcomes for 4 categories of interventions: sound therapies, repetitive transcranial magnetic stimulation (rTMS), cognitive behavioral therapy (CBT), and tinnitus-specific interventions that combined psychological counseling with sound therapy. We selected randomized controlled trials (RCTs) or controlled clinical trials; we also allowed cohort studies with a concurrent control group for safety outcomes, and cost analyses for cost outcomes. For efficacy outcomes, we only selected studies that reported using validated measures of tinnitus distress or disability, psychological outcomes, or quality of life outcomes.

Data Extraction: One research team member extracted data and a second checked for accuracy. Two investigators independently assessed the risk of bias of included studies. We rated the certainty of the evidence using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach.

Data Synthesis: We included 59 RCTs or controlled trials; some studies included multiple intervention arms. All but 1 study reported measures of tinnitus distress and disability; 16 studies reported safety outcomes, and 1 study reported cost outcomes. Eleven studies reported on the impact of sound therapies (hearing aids with sound generators, sound maskers, altered auditory stimuli, auditory attention training) compared to sham controls; overall minimal to no effect was observed on most measures of tinnitus-related distress or disability and psychological measures. Nineteen RCTs reported on the impact of rTMS compared to sham stimulation; overall minimal to no effect was observed on most measures of tinnitus-related distress or disability, psychological measures, or quality of life. Fourteen of the 19 RCTs also reported safety outcomes and findings were mixed across studies. Twenty-one RCTs reported on the impact of therapist-led individual- or group-based CBT, or internet- or book-guided CBT compared to delayed treatment or attention control groups. Findings suggested a favorable benefit of interventions on measures of tinnitus distress and disability and some psychological measures, but the magnitude of benefit could not be precisely estimated because of heterogeneity in outcome ascertainment and reporting. Ten RCTs reported on the impact of tinnitus-specific interventions, mainly tinnitus retraining therapy that combines psychological counseling with sound therapy. Findings suggested a favorable benefit on some measures of tinnitus distress and disability.

Limitations: In this HTA, we focused on the most common non-invasive, non-pharmacologic interventions that were published in peer-reviewed journals. Nearly all studies had some concerns for bias or were high risk for bias; additionally, sample sizes were small in many studies leading to imprecise estimates of effect. Interventions, study designs, and outcomes reported within each intervention category were heterogenous. This evidence base offered no information about the effectiveness of treatment in subpopulations of interest, including those with occupational noise exposure.

Conclusions: CBT interventions, or tinnitus-specific interventions that combine psychological counseling with sound therapy may offer some benefit for reducing tinnitus-related distress and disability. Sound therapy alone and rTMS interventions in their current state may not be effective; additional research may be needed to refine these interventions. There may be few to no harms from most CBT and sound therapy interventions; the evidence is insufficient to determine harms from rTMS interventions. Evidence is lacking with respect to cost outcomes.

ES 1. Background

We designed this health technology assessment (HTA) to assist the State of Washington's independent Health Technology Clinical Committee with determining coverage for non-invasive, non-pharmacologic treatments for tinnitus.

ES 1.1 Condition Description

Tinnitus refers to the auditory experience of ringing, buzzing, roaring, or hissing in the ears. The experience of tinnitus is very heterogeneous in terms of the type of sound, intensity (e.g., pulsatile or rhythmical), frequency (e.g., constant or intermittent), and location (e.g., one or both ears) of the perceived sound.[1] Once secondary causes for tinnitus have been ruled out or addressed, the treatment for tinnitus is aimed reducing the perception of tinnitus, or reducing reactions to the tinnitus, or both. Because tinnitus is largely subjective, outcomes related to tinnitus treatment are typically self-reported. Further, experts suggest that because tinnitus is heterogenous, no one treatment may be effective for all individuals.[2,3]

ES 1.2 Disease Burden

Based on nationally representative data from the National Health and Nutrition Examination Survey (NHANES) from the past 2 decades, the prevalence of tinnitus in adults has ranged from 7.1% to 14.6%.[4,5] Tinnitus can result in comorbidities that include depression, anxiety, hearing and concentration difficulties, and sleep disturbance, all of which may negatively impact a person's overall quality of life.[6,7]

ES 1.3 Technology Description

This HTA includes an evaluation of 1) sound therapies, 2) repetitive transcranial magnetic stimulation (rTMS), 3)cognitive behavioral therapy (CBT), and 4) tinnitus-specific therapies that combine psychological counseling and sound therapy as part of a multicomponent intervention for the treatment of subjective tinnitus that is bothersome.

ES 1.3.1 Sound Therapies

This category includes sound generators, sound maskers, altered auditory stimuli (e.g., listening to frequency-altered music), and hearing aids that may incorporate sound-masking or sound-generating features.

ES 1.3.2 Repetitive Transcranial Magnetic Stimulation (rTMS)

rTMS is a neuromodulation intervention that involves the delivery of multiple electromagnetic pulses to the scalp that are targeted to specific brain regions, temporoparietal or temporal in the case of tinnitus. These pulses are delivered over multiple sessions over the course of days to weeks.

ES 1.3.3 Cognitive Behavioral Therapy (CBT)

CBT describes a specific psychotherapy approach used for a variety of mental health and other disorders that is based on cognitive restructuring and behavior modification. For tinnitus, CBT principles are used to promote changes to reduce the distress associated with tinnitus.[8]

ES 1.3.4 Tinnitus-Specific Therapies

Other interventions that combine components of sound therapy and psychological therapy have also been used for the treatment of tinnitus. These include tinnitus retraining therapy (TRT), neuromonics tinnitus treatment (NTT), tinnitus activities treatment (TAT), tinnitus-masking counseling, and others.

ES 1.4 Regulatory Status

As of 2019, the U.S. Food and Drug Administration (FDA) has approved 72 sound-masking/generating devices through its 510k clearance process. The FDA has approved rTMS for use in treating several conditions including treatment-resistant depression (2008), acute migraine headache (2013), and obsessive-compulsive disorder (2018).[9] Tinnitus is not an approved rTMS indication.

ES 1.5 Policy Context

The State of Washington HCA selected this topic for review because of medium concerns for safety and high concerns for efficacy and cost.

ES 1.6 Washington State Agency Utilization Data

Utilization data from the state are pending.

ES 2. Methods

This section describes the methods we used to conduct this HTA.

ES 2.1 Research Questions and Analytic Framework

We developed the following research questions to guide this HTA:

Key Question 1: Effectiveness (Health Outcomes)

1. What is the effectiveness of non-invasive, non-pharmacologic therapies for the treatment of bothersome, subjective tinnitus?

Key Question 2: Safety

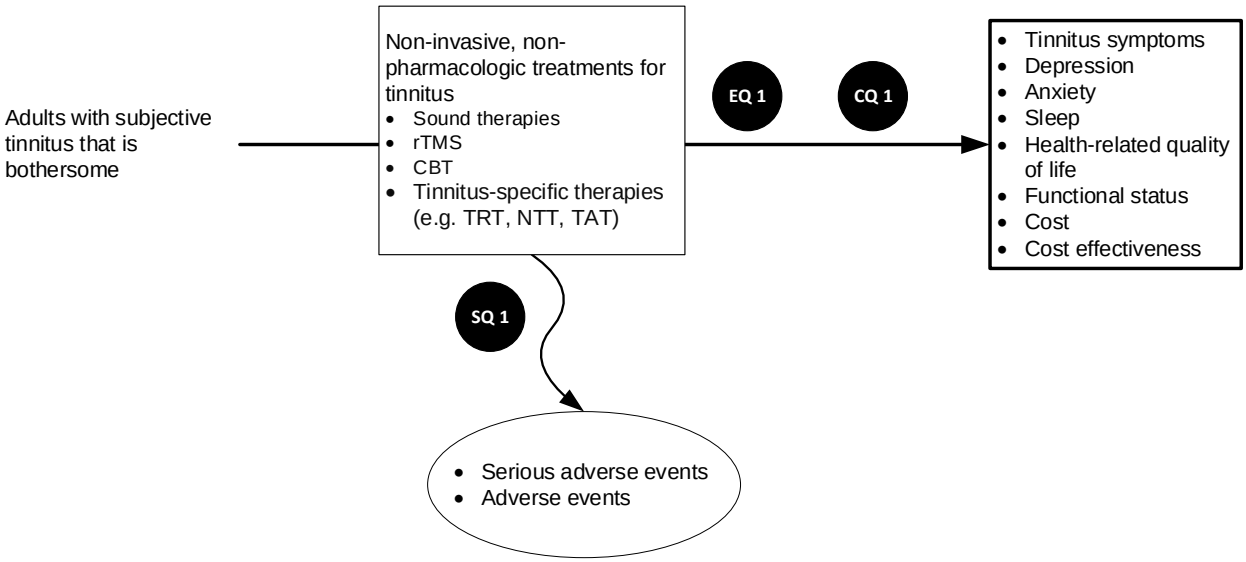
2. What are the harms associated with non-invasive, non-pharmacologic therapies for the treatment of bothersome, subjective tinnitus?

Key Question 3: Cost

3. What are the costs and cost-effectiveness of non-invasive, non-pharmacologic therapies for the treatment of bothersome, subjective tinnitus?

We also created the analytic framework, shown in ***Figure ES-1***, to guide our review.

Figure ES-1. Analytic framework for Health Technology Assessment on Non-pharmacologic, Non-invasive Treatments for Tinnitus



Abbreviations: CBT = cognitive behavioral therapy; CQ = cost question; EQ = effectiveness question; NTT = neuromonics tinnitus treatment; rTMS = repetitive transcranial magnetic stimulation; SQ = safety question; TAT= tinnitus activities treatment; TRT = tinnitus retraining therapy.

ES 2.2 Data Sources and Search

We searched PubMed, EMBASE, PsycINFO, and the Cochrane Library for relevant studies published in English from database inception to September 9, 2019. In addition, we reviewed the reference lists of relevant studies, systematic reviews, practice guidelines on the topic to identify any relevant primary research studies that were not found through the electronic database search.

ES 2.3 Study Selection

Two reviewers independently screened titles and abstracts and full-text articles based on the following study inclusion criteria (complete details are in ***Table*** of the Full Technical Report).

- **Population:** Adults with subjective tinnitus that is bothersome and whose tinnitus is described as primary, idiopathic, or neurophysiologic.
- **Intervention:** Sound generators or maskers, hearing aids with specific sound generating features, rTMS, CBT, tinnitus-specific interventions that included psychological counseling with sound therapy.
- **Comparator(s):** No treatment, usual care, waitlist (i.e., delayed treatment), or sham treatment.
- **Outcomes:** Validated measures of tinnitus symptoms, distress, or disability, validated psychological measures (depression, anxiety, sleep impact, overall mental health or well-being), validated health-related quality of life measures; safety and harms (serious adverse events, adverse events, side effects including device-related complications), and cost outcomes (costs of intervention and cost-effectiveness).
- **Setting(s):** Primary or specialty care settings in countries with a development rating designated as *very high* on the United Nations Human Development Index.[10]
- **Study Design:** Randomized controlled trials (RCTs), controlled clinical trials, observational cohort studies with a concurrent control group (for safety outcomes only), cost-benefit analyses, cost-utility analyses, or cost-effectiveness analyses.
- **Other:** English-language.

This review did not include studies focused on the comparative effectiveness of various interventions. Studies evaluating multiple interventions were only included if an eligible comparator group was also included and only data from eligible comparisons were considered for inclusion in this HTA. For practical purposes, we excluded less commonly used non-invasive treatments. Comparative effectiveness studies and studies of less commonly used treatments are cataloged in ***Appendix G*** of the full report.

ES 2.4 Data Abstraction and Risk of Bias Assessment

Two team members extracted relevant study data into a structured abstraction form, and a senior investigator checked those data for accuracy. Two team members conducted independent risk of bias assessments on all included studies. Risk of bias was assessed as *high*, *some concerns*, or *low* using the Cochrane 2.0 Risk of Bias instrument.[11]

ES 2.5 Data Synthesis and Quality of Evidence Assessment

We summarized continuous outcome measures as absolute mean differences (AMDs) between treatment groups where possible and summarized categorical outcomes using absolute (risk difference [RD]) and relative (risk ratio [RR]) for between-group differences in proportions. We calculated effects and conducted statistical significance testing when authors did not report it and the data were available in the article. We qualitatively synthesized study characteristics and results for each research question by intervention category in tabular and narrative formats. We graded the certainty of the evidence for each comparison and category of outcomes using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach.[12]

ES 3. Results

We included a total of 59 studies reported in 65 articles published between 1996 and 2019. Fifty-eight studies provided evidence on effectiveness (EQ 1), 16 studies provided evidence for safety outcome (SQ 1), and 1 study provided evidence on cost outcomes (CQ 1).

ES 3.1 Outcomes Evaluated

Studies included in this HTA used a variety of validated instrument and scales to measure the effectiveness of tinnitus treatment across a range of outcome domains. ***Table 3*** in the full technical report summarizes the measures used to assess the effect of treatment on tinnitus-related distress and disability, and ***Table 4*** in the full report summarizes the measures used to assess the impact on psychological symptoms, sleep, and quality of life (QoL).[13,14] A clinically meaningful difference has been established for some, but not all of the measures used by included studies.

ES 3.2 Sound Therapy Interventions

We identified 11 RCTs described in 13 publications that focused on sound therapy.[15-25] The following 4 comparisons were represented in this body of evidence: 1) hearing aids with sound generating features compared to standard hearing aids, 2) altered auditory stimulus compared to sham stimulus, 3) sound generators with counseling, education, or information compared to those interventions without sound generators, and 4) auditory attention training game compared to a sham training game. One of the studies[24] included in this category also featured an eligible tinnitus-specific intervention in addition to the sound therapy intervention; the results from the tinnitus-specific intervention are detailed in the tinnitus-specific therapies section of this report (Section 3.5). Key findings are:

- All studies reported measures of tinnitus distress or disability, which were the primary outcomes in nearly all trials. Most studies reported no significant differences between intervention and control groups; however, studies involving auditory stimulus interventions observed mixed findings. Among the 4 studies evaluating this type of intervention, 2 studies reported a statistically significant difference in measures of tinnitus distress or disability, favoring the intervention, whereas 2 observed no statistically significant differences.

- Two RCTs[17,19] reported on psychological measures. No statistically significant differences were measured between intervention and control groups in either of the 2 trials.
- One RCT[20] reported adverse events, which were not significantly different between the intervention group and control group.
- No RCT reported on cost outcomes.

ES 3.3 Repetitive Transcranial Magnetic Stimulation Interventions

We identified 10 parallel-assignment RCTs[26-35] and 9 crossover RCTs[36-44] from 19 publications describing results of rTMS stimulation interventions compared to sham stimulation. These interventions varied in terms of the number of sessions used, the duration over which the sessions were provided, and the timing of outcome measure follow-up. Key findings are:

- Eighteen RCTs[26-36,38-44] reported measures of tinnitus distress or disability, which were the primary study aims in most studies. Most studies demonstrated no statistically significant differences in measures of tinnitus distress and disability between active rTMS and sham rTMS.
- Five RCTs[30,32,34,39,41] reported psychological measures. All studies demonstrated no statistically significant differences between active rTMS and sham rTMS in depression, anxiety, or sleep outcomes.
- One RCT[32] reported on quality of life and reported no difference between active rTMS and sham rTMS.
- Fourteen RCTs[26,28-34,36-41] reported on adverse events. Five studies reported no adverse events in either the active rTMS or sham rTMS groups, and 3 studies reported some adverse events but did not report by group. Of the remaining 6 studies, 3 reported a similar incidence of adverse events between groups, 2 reported a higher incidence of events among the active rTMS group, and 1 reported a higher incidence among the sham rTMS group.
- No RCT reported cost outcomes.

ES 3.4 Cognitive Behavioral Therapy Interventions

We identified 21 studies that described CBT interventions for the treatment of tinnitus, of which 19 were RCTs,[45-63] 1 was a cluster RCT,[64] and 1 was a controlled trial.[65] Nearly all studies used wait list control groups (i.e., delayed treatment), though some studies also included attention control groups. One of the RCTs evaluated tinnitus retraining therapy (TRT) in addition to a CBT intervention; the results for the TRT intervention arm are included in Section 3.5 of this report.[58] The key findings for CBT are:

- Thirteen RCTs[45,47,49,50,53,54,56-58,62,63,65,66] reported on group or individual, therapist-led CBT interventions. These interventions improved tinnitus-related distress and disability in a majority of studies, although findings were somewhat heterogenous across measures used.
- Nine RCTs[46,48-52,55,60,64] evaluated internet or book-guided self-directed interventions. These interventions also improved measures of tinnitus distress and disability compared to control, although findings were also heterogenous across measures and follow-up timepoints assessed.

- In 11 RCTs[45,49,50,53,54,56,57,59,61-63] that investigated therapist-led CBT interventions and that reported on psychological outcomes, most favored the intervention, although findings were only statistically significant in some studies.
- In 8 RCTs[46,48-51,55,60,64] that used internet or book-guided CBT and that reported on psychological outcomes, most favored the intervention, although findings were only statistically significant in some studies.
- In 2 RCTs[51,64] that used internet or book-guided CBT and that reported on QoL, no statistically significant findings between intervention and control were observed. No studies of therapist-led CBT reported QoL outcomes.
- In 3 RCTs[54,61,65] that used therapist-led interventions and that reported on adverse events, the frequency of adverse events was rare to none.
- No RCTs reported on cost outcomes.

ES 3.5 Tinnitus-specific Interventions

We identified 10 RCTs reported in 11 publications describing results from studies that focused on tinnitus-specific therapies.[24,58,67-74] The interventions evaluated included tinnitus retraining therapy (8 studies[58,67-73]), neuromonics treatment (1 study[24]), and a tinnitus retraining music-based therapy (1 study[74]). One study that evaluated TRT also included an additional tinnitus-specific intervention called tinnitus masking.[67] In addition to the tinnitus-specific interventions evaluated, 1 study also included an eligible sound therapy study arm,[24] and 1 study included an eligible CBT intervention study arm.[58] Results for those 2 study arms are reported in the sound therapy (Section 3.2) and CBT (Section 3.4) sections of this report, respectively. Key findings are:

- All studies reported measures of tinnitus distress or disability as the primary outcome. Eight studies found statistically significant favorable effects of the intervention on at least 1 measure; however, the significance and magnitude of the effect varied by measure, timepoint, and comparison group. One study did not conduct significance testing but found a larger improvement in the intervention group and the remaining study found no statistically significant difference in effect, on this or any other type of tinnitus-specific measure.
- Three RCTs[68-70] reported on psychological measures. Two studies found statistically significant favorable effects for the intervention on some measures or time points but not all, and the third study found no difference in effect between intervention and control group, which was consistent with other measures reported from this study.
- Two RCTs[68,69] reported on quality of life measures. One study found no difference in effect between intervention and control group, which was consistent with all other measures reported from this study. The second study found larger statistically significant improvements in the intervention group at 8 and 12 months for the intervention group compared to the control group.
- One RCT[68] that compared tinnitus retraining therapy to usual care over 8 months duration reported safety and cost outcomes. This study reported that no adverse events occurred, and the cost per quality-adjusted life year (QALY) gained from health care payor perspective was

$10,456 (95% CI, NR), with 58% to 68% probability of being cost-effective using a $45,000 willingness to pay threshold.

ES 4. Discussion

ES 4.1 Summary of the Evidence

The certainty of evidence (i.e., GRADE rating) for the effectiveness of the interventions included in this HTA ranged from very low to low. A summary of the certainty ratings is provided in ***Table ES-1***; detailed GRADE ratings are provided in ***Appendix H*** of the full report. The findings from this HTA are largely consistent with findings from other systematic reviews on the treatment of tinnitus.[75-82]

Table ES-1. Summary of GRADE Certainty Ratings for Non-invasive, Non-pharmacologic Interventions for Tinnitus Included in This HTA

Intervention (Comparison)	Outcome	No. Studies (No. Participants)	Certainty of Evidence[a]	Direction
Sound therapy interventions				
Hearing aids with sound-generating features (regular hearing aids)	Tinnitus distress and disability	3 RCTs (87)	●○○○	No benefit
Altered auditory stimulus (control stimulus)	Tinnitus distress and disability	4 RCTs (219)	●○○○	Unable to determine
	Psychological measures	1 RCT (50)	●○○○	No benefit
	Safety	1 RCT (100)	●○○○	No harms
Sound generators with information, education, counseling (information, education, counseling alone)	Tinnitus distress and disability	3 RCTs (234)	●○○○	No benefit
	Psychological measures	1 RCT (48)	●○○○	Unable to determine
Auditory Attention Training Game (control game)	Tinnitus distress and disability	1 RCT (31)	●○○○	Unable to determine
Repetitive transcranial magnetic stimulation interventions				
Active rTMS (sham rTMS)	Tinnitus distress and disability	18 RCTs (760)	●●○○	No benefit
	Psychological measures	5 RCTs (247)	●○○○	No benefit
	Quality of life	1 RCT (153)	●○○○	No benefit
	Safety	14 RCTs (526)	●○○○	Unable to determine
Cognitive behavioral therapy interventions				
Therapist-led individual or group CBT interventions (delayed treatment or attention control)	Tinnitus distress and disability	13 RCTs (1,743)	●●○○	Benefit
	Psychological measures	11 RCTs (1,100)	●●○○	Benefit
	Safety	3 RCTs (436)	●●○○	No harms
Internet or book-guided CBT interventions (delayed treatment or attention control)	Tinnitus distress and disability	9 RCTs (946)	●●○○	Benefit
	Psychological measures	8 RCTs (784)	●●○○	Benefit
	Quality of life	2 RCTs (120)	●○○○	No benefit
Tinnitus-specific interventions (tinnitus retraining therapy and others)				
Tinnitus-specific interventions with sound therapy (delayed treatment or attention control)	Tinnitus distress and disability	7 RCTs (937)	●●○○	Benefit
	Psychological measures	2 RCTs (556)	●○○○	Unable to determine
	Quality of life	2 RCTs (556)	●○○○	Unable to determine

	Safety	1 RCT (492)	⊕◯◯◯	Unable to determine
	Cost	1 RCT (492)	⊕◯◯◯	Unable to determine
Tinnitus-specific interventions without sound therapy (delayed treatment or attention control)	Tinnitus distress and disability	3 RCTs (409)	⊕◯◯◯	Benefit
	Psychological measures	1 RCT (90)	⊕◯◯◯	Unable to determine

Notes: [a]Certainty ratings: ⊕◯◯◯ Very low, ⊕⊕◯◯ Low, ⊕⊕◯◯ Moderate. ⊕⊕⊕⊕ High

Abbreviations: CBT = cognitive behavioral therapy; RCT = randomized controlled trial; rTMS = repetitive transcranial magnetic stimulation.

ES 4.2 Limitations of the Evidence Base

This HTA included many RCTs with high risk of bias and studies with small sample sizes resulting in imprecise effect estimates. The sources of bias varied across studies, but lack of robust randomization and allocation concealment processes or description of baseline characteristics reported by group to assess the adequacy of randomization was a common issue. Studies using delayed treatment controls could not be blinded, and because patient-reported outcomes were used, outcome assessment could also not be blinded. Though most rTMS trials were blinded, many were crossover trials and the process of motor threshold titration to determine stimulation intensity compromises the blinding in such studies. Few trials were conducted according to a prespecified protocol and analysis plans, increasing the risk for reporting bias. Some studies had high attrition rates or did not report sufficient information to be able to assess attrition. Interventions and study designs were heterogenous across all intervention categories. This may reflect the challenge involved in treating a heterogenous condition, and the evolving search for effective treatments. Lastly, the evidence provided no information about the effectiveness of treatments in subpopulations of particular interest, including those with occupational exposure to noise.

ES 4.3 Clinical Practice Guidelines

We identified 5 clinical practice guidelines (CPGs) related to the treatment of tinnitus and rated them using the Appraisal of Guidelines for Research & Evaluation II (AGREE) instrument.[83,84] With this tool, guidelines are assigned an overall score from 1 (lowest quality) to 7 (highest quality). We assessed all CPGs as a "4" or higher using this tool. One guideline was specific to persons with mild traumatic brain injury (no recommendations for any particular treatment),[85] and another was specific to only rTMS interventions across a variety of clinical conditions.[79] The 3 broader guidelines were generally consistent in their recommendations. All recommended the use of CBT for the treatment of tinnitus.[86-88] Two recommended against rTMS, while the third reported 'no recommendation for or against" rTMS. Two of the 3 guidelines had no recommendation for or against sound therapy, while 1 considered sound therapy as a potential option. Hearing aids were recommended by 2 guidelines but only for persons with hearing loss. Detailed descriptions of the CPGs are in ***Table 10*** of the Full Technical Report.

ES 4.4 Selected Payer Coverage Policies

Table ES-2 provides an overview of selected payer coverage policies for tinnitus. Prior to 2014, a CMS National Coverage Determination (NCD) stated that tinnitus maskers (i.e., sound therapy) was considered experimental and was therefore not covered. However, effective

December 18, 2014,[89] CMS removed the tinnitus NCD. As a result, there is no stated CMS policy on tinnitus treatment. Other than Cigna, which covers CBT to "address psychosocial, behavioral, and emotional impairments and to improve occupational performance," most commercial payers either do not have a specific policy or do not cover the tinnitus treatments included in the scope of this HTA.

Table ES-2. Overview of Payer Coverage Policies for Tinnitus

Treatment Type	Medicare	Medicaid	Aetna	Cigna	Humana	Kaiser Permanente	Premera Blue Cross	Regence BlueShield	TRICARE	UnitedHealth
CBT	—	—	x	✓[a]	x	—	—	—	—	—
rTMS	—	—	x	x	x	—	—	x	—	x
Sound Therapy	—	—	x	—	x	x	—	—	x	x
Tinnitus-Specific Interventions	—	—	x	—	x	x	—	—	—	—

Notes: ✓ = covered when specific criteria have been met; ✕ = not covered; — = no policy identified; [a] This treatment would likely be covered on a case-by-case basis, as it pertains to moderate to severe traumatic brain injury and does not specifically address tinnitus; however, the policy specifically notes the use of CBT interventions to "address psychosocial, behavioral, and emotional impairments and to improve occupational performance."

Abbreviations: CBT = cognitive behavioral therapy; rTMS = repetitive transcranial magnetic stimulation.

ES 4.5 Limitations of this HTA

This HTA was limited to peer-reviewed studies published in English. We did not include data or results presented solely in conference abstracts. Our effectiveness question did not include comparative effectiveness of interventions. Further, we did not include studies of neuromodulation therapies other than rTMS, and psychological interventions other than CBT were only included if part of a combined psychological-sound therapy intervention. We did not include other kinds of non-invasive interventions that might be used to treat tinnitus such as alternative and complementary therapies or lifestyle modifications. Pharmacologic treatment and invasive interventions were also outside the scope of this HTA.

ES 4.6 Ongoing Research

We identified 35 relevant ongoing trials of the types of interventions included in this HTA from the ClinicalTrials.gov trial registry. Some list estimated completion dates in 2019 but have not yet published results.

ES 5. Conclusion

CBT interventions, or tinnitus-specific interventions that combine psychological counseling with sound therapy may offer some benefit for reducing tinnitus-related distress and disability. Sound therapy alone and rTMS interventions in their current state may not be effective; additional research may be needed to refine these interventions. There may be few to no harms from most CBT and sound therapy interventions; the evidence is insufficient to determine harms from rTMS interventions. Evidence is lacking with respect to cost outcomes.

Full Technical Report

1. Background

We conducted this health technology assessment (HTA) to assist the State of Washington's independent Health Technology Clinical Committee with determining coverage for non-invasive, non-pharmacologic treatments for tinnitus.

1.1 Condition Description

Tinnitus refers to the auditory experience of ringing, buzzing, roaring, or hissing in the ears. The experience of tinnitus is very heterogeneous in terms of the type of sound, intensity (e.g., pulsatile or rhythmical), frequency (e.g., constant or intermittent), and location (e.g., one or both ears) of the perceived sound.[1] There are two main types of tinnitus: objective and subjective. In objective tinnitus, which is very rare (<1% of tinnitus cases), the sounds have an origin within the patient's body and both the patient and examiner perceive them. In subjective tinnitus, only the patient perceives the sounds, and the sounds are not associated with an underlying condition that might explain the sound. This type of tinnitus is often associated with hearing loss. Because tinnitus is largely subjective, outcomes related to tinnitus treatment are typically self-reported.

In addition to being characterized as objective or subjective, tinnitus can also be classified as primary or secondary. Secondary tinnitus may result from underlying vascular disorders, tumors or other structural brain malformations (e.g., Chiari malformation), eustachian tube dysfunction, ototoxic medications, and other somatic disorders. In contrast, primary tinnitus is typically neurologic in origin, commonly accompanying sensorineural hearing loss or dysfunction within the auditory system. Further, experts suggest that because tinnitus is heterogenous, no one treatment may be effective for all individuals.[2,3] Thus, group-level data from treatment studies may not reflect the experience among individuals or selected subgroups.[90]

1.2 Disease Burden

Based on nationally representative data from the National Health and Nutrition Examination Survey (NHANES) from the past 2 decades, the prevalence of tinnitus in adults has ranged from 7.1% to 14.6%.[4,5] In a 10-year prospective, community-based study in Wisconsin that followed 2,922 participants free of tinnitus at baseline, the 10-year cumulative incidence was 12.7%.[91] The prevalence of tinnitus increases with age, and risk factors include hypertension, smoking, loud leisure-time, firearm, and occupational noise exposure.[4]

Tinnitus can result in comorbidities that include depression, anxiety, hearing and concentration difficulties, and sleep disturbance, all of which may negatively impact a patient's overall quality of life.[6,7]. Among respondents to the 2007 National Health Interview Survey who reported tinnitus, 36% had nearly constant symptoms, 15% reported daily symptoms, another 15% reported weekly symptoms, and 34% reported symptoms less than weekly.[92] Additionally, 27% had symptoms for longer than 15 years. Almost a third of respondents were not bothered by their tinnitus, but more than a quarter thought it to be a very big, big, or moderate problem.

Approximately half of the respondents with tinnitus had not discussed their tinnitus with a physician.[92]

There is a relationship between tinnitus and mental health disorders, particularly depression and anxiety.[93-97] In the 1999-2004 National Health and Nutrition Examination Survey, people with generalized anxiety disorder (GAD) or major depressive disorder (MDD) were more likely to report having any tinnitus than people without GAD or MDD (odds ratio [OR] 2.7; 95% confidence interval [CI] 1.3 to 5.3 for GAD and OR 2.0; 95% CI 1.2 to 3.3 for MDD).[4] Sleep disturbances are also very common among patients with tinnitus, though the relationship is not clearly understood. Sleep impairment is often correlated with more severe tinnitus, and both negatively impact overall quality of life.[98-100] One mechanism for the relationship between sleep and tinnitus is thought to be hyperarousal due to the overactivation of the sympathetic nervous system.[7,101]

The psychological model proposed by Tyler, Aran, and Dauman suggests that overall tinnitus annoyance is a result of tinnitus characteristics and the psychological make up of each individual person, and that several parts of the brain are involved in the representation of tinnitus and the person's reaction to it.[102] Once secondary causes for tinnitus have been ruled out or addressed, the treatment for tinnitus is aimed reducing the perception of tinnitus, or reducing reactions to the tinnitus, or both.

Tinnitus is a significant financial burden on health care systems and society, especially since there is no known organic cause of subjective tinnitus or a singular effective treatment. The authors of an economic analysis of tinnitus management summarized data from a Dutch study[103] and reported an average annual cost of chronic tinnitus of $2,110 (U.S. dollars[USD]) and an annual productivity cost of over $5,000. The authors of a retrospective chart review and patient satisfaction questionnaire from patients at a large Midwestern hospital reported a mean annual cost of $662.60 USD (range: $53 to $10,049) per patient.[104]

1.3 Technology Description

For this HTA, we focused on the most commonly used or evaluated therapies for subjective, bothersome tinnitus. These therapies include sound treatment (e.g., sound maskers or generators), repetitive transcranial magnetic stimulation (rTMS), cognitive behavioral therapy (CBT), and other tinnitus-specific therapies, which typically combine psychological and sound therapy as part of a multi-component intervention.

1.3.1 Sound Therapies

Sound therapy for tinnitus is broadly described as the use of sound to alter a patient's perception of and reaction to tinnitus sounds.[8,105] Habituation to tinnitus by reducing the contrast between the tinnitus sound and environmental sounds is 1 mechanism of sound therapy. Other potential mechanisms of sound therapy are to instill a sense of relief by exposing the patient to soothing sounds or to distract the patient from the tinnitus sounds. Habituation can be achieved through the use of sound generators or maskers that emit noise or mask noise; such devices can be used at the ear-level through ear pieces or headphones, or can be incorporated into hearing aids as an

additional feature to standard amplification, or can emit sound into the ambient environment. In addition to standard sound generation, variations of sound therapy include use of noise or music stimuli that has been audiologically altered to emit noise at specific frequencies, often matched to the person's tinnitus frequency to reduce perception of the bothersome tinnitus. Numerous sound therapy devices have been FDA-approved (See Section 1.4).

1.3.2 Repetitive Transcranial Magnetic Stimulation

Repetitive transcranial magnetic stimulation (rTMS) is the main non-sound therapy-based neuromodulation technique being studied for the treatment of tinnitus.[106,107] The goal of rTMS is to decrease neuronal hyperactivity by inducing electrical currents in specific areas of the brain. With rTMS, a coil that is in contact with the patient's scalp delivers multiple electromagnetic pulses over a specific length of time (i.e., a session). rTMS is typically provided over multiple sessions over the course of days to weeks. The low-frequency pulses directed at the temporal or temporoparietal cortical areas of the brain area are meant to reduce neural activity in regions thought to be involved with perception of tinnitus; however, other target areas of the brain and frequency of pulses are under evaluation. The therapeutic effect of rTMS, however, is thought to be partial and temporary.[78] rTMS is not FDA-approved for the treatment of tinnitus but is approved for the management of treatment-resistant depression, acute migraine headache, and obsessive-compulsive disorder.

1.3.3 Cognitive Behavioral Therapy

Cognitive behavioral therapy (CBT) describes a psychotherapy approach used for a variety of mental health and other disorders that is based on cognitive restructuring and behavior modification. The first application of CBT for tinnitus was described in 2000.[108] For tinnitus, CBT principles are used to promote changes to reduce the distress associated with tinnitus.[8] Specific goals of CBT for tinnitus include reducing attention on the tinnitus sounds, reconsidering tinnitus and its consequences, and improving coping skills. The approach to using CBT for the treatment of tinnitus can vary in several ways including duration and intensity of treatment, mode of delivery (in person, group, virtual), and fidelity to CBT principles and treatment protocol.

1.3.4 Other Tinnitus-Specific Therapies

Other interventions that combine components of sound therapy and psychological therapy have also been used for the treatment of tinnitus. We will consider them separately from sound therapy or CBT interventions in this HTA because they were developed specifically as multicomponent interventions, and some are recognized by specific names that distinguish them as unique interventions.

Tinnitus retraining therapy (TRT) is a two-component treatment that combines directive counseling with supplemental sound masking just below the perceived level of tinnitus to relieve tinnitus symptoms.[8,109] Counseling sessions, the treatment regimen's primary focus, are intensive and individualized, and center on demystifying tinnitus and educating patients about the condition's physiological mechanisms. The secondary element is sound therapy, which uses constant broadband sound to mask tinnitus noise. Together, the counseling and sound masking

are meant to achieve habituation to the tinnitus sounds and decrease the annoyance the tinnitus sounds often evoke.[109]

Other examples of tinnitus-specific interventions include Neuromonics Tinnitus Treatment (NTT), a proprietary acoustic desensitization treatment that employs customized acoustic stimuli (comprised of music and noise). Over the course of approximately 6 months, patients receive 2 to 3 hours of neurological stimulation each day, delivered via a small headset device that resembles an MP3 player. As part of the program, patients are also seen periodically by a trained audiologist for counseling.[110,111] Tinnitus Activities Treatment (TAT) is another example of a tinnitus-specific intervention. The 3 main components of TAT are informal counseling, activities engagement, and sound therapy (as needed).[8,112]

Progressive tinnitus management (PTM) was developed by the U.S. Veterans Administration's National Center for Rehabilitative Audio Research.[8] Rather than being a specific therapy, PTM is an incremental care delivery strategy for tinnitus diagnosis and treatment that involves (1) referral to audiology, (2) audiologic evaluation, (3) audiology and mental health skills education, (4) interdisciplinary evaluation (ideally with a psychologist or psychiatrist), and (5) individualized support with a goal of teaching self-efficacy skills.[113] In this HTA, we categorized studies evaluating PTM based on the primary treatment modality used (e.g., CBT, tinnitus-specific intervention).

1.4 Regulatory Status

Some of the technologies evaluated in the scope of this HTA are devices regulated by the U.S. Food and Drug Administration (FDA), including sound devices and rTMS. As of 2019, the FDA has approved 72 sound-masking devices through the 510k clearance process as detailed in ***Appendix B***, ***Table B1***.[114] The FDA has approved rTMS for use in treating several conditions including treatment-resistant depression (2008), acute migraine headache (2013), and obsessive-compulsive disorder (2018).[9] In addition, the FDA issued guidance to industry regarding rTMS systems in 2011.[115] Tinnitus is not an approved rTMS indication.

1.5 Policy Context

The State of Washington Health Care Authority selected non-invasive, non-pharmacologic treatments for tinnitus for an HTA because of medium concerns of safety and high concerns for efficacy and cost.

1.6 Washington State Agency Utilization Data

Data from the state are pending.

2. Methods

This section describes the methods we used to conduct this HTA.

2.1 Research Questions and Analytic Framework

We developed the following research questions to guide the systematic evidence review of primary research studies:

Key Question 1: Effectiveness (Health Outcomes)

1. What is the effectiveness of non-invasive, non-pharmacologic therapies for the treatment of bothersome, subjective tinnitus?

Key Question 2: Safety

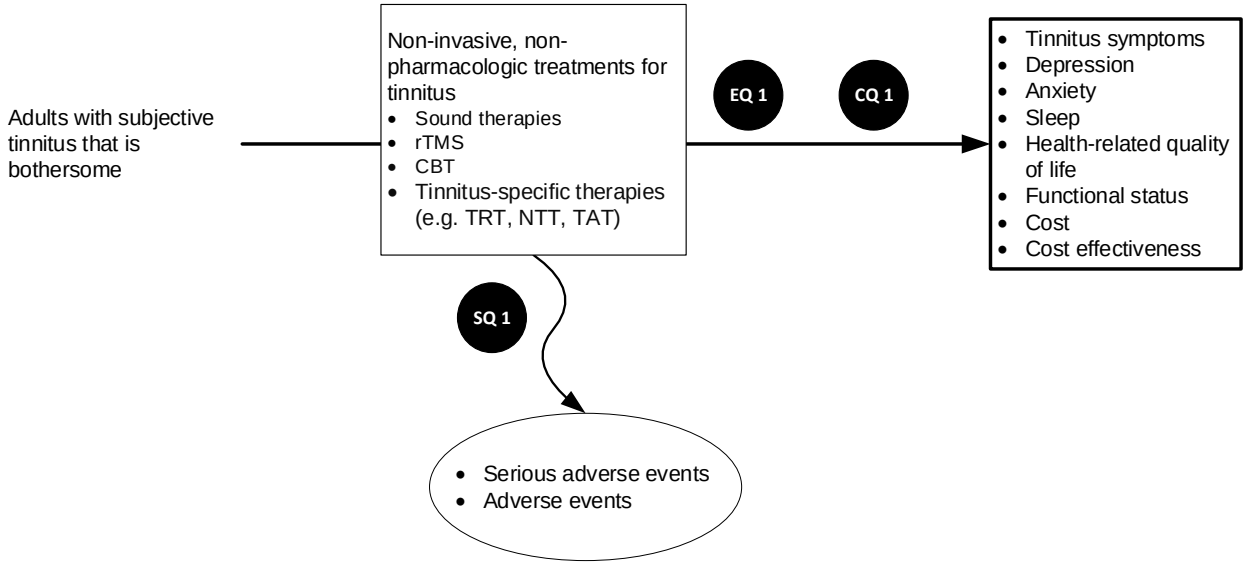
2.: What are the harms associated with non-invasive, non-pharmacologic therapies for the treatment of bothersome, subjective tinnitus?

Key Question 3: Cost

3: What are the costs and cost-effectiveness of non-invasive, non-pharmacologic therapies for the treatment of bothersome, subjective tinnitus?

We also created the analytic framework, shown in ***Figure 1***, to guide our review.

Figure 1. Analytic framework for Health Technology Assessment on Non-pharmacologic, Non-invasive Treatments for Tinnitus



Abbreviations: CBT = cognitive behavioral therapy; CQ = cost question; EQ = effectiveness question; NTT = neuromonics tinnitus treatment; rTMS = repetitive transcranial magnetic stimulation; SQ = safety question; TAT = tinnitus activities treatment; TRT = tinnitus retraining therapy.

The State of Washington HTA Program posted a draft of these research questions with study selection criteria for public comment from October 10 to October 23, 2019. The final key questions and response to public comments on the draft key questions were published on

November 7, 2019 and are available at the Program's website (https://www.hca.wa.gov/about-hca/health-technology-assessment/tinnitus-non-invasive-non-pharmacologic-treatments).

2.2 Data Sources and Searches

We searched PubMed, EMBASE, PsycINFO, and the Cochrane Library for relevant studies published in English from inception to September 9, 2019. To ensure comprehensive identification of studies of relevant interventions, we used medical subject headings (MeSH terms), MeSH subheadings, and keyword terms. The detailed electronic search strategy is presented in ***Appendix C***. In addition, we reviewed the reference lists of relevant studies, systematic reviews, practice guidelines, and other HTAs on the topic to identify any relevant primary research studies that were not found through the electronic search.

2.3 Study Selection

Table 1 summarizes the study selection criteria related to the populations, interventions, comparators, outcomes, study time periods, study design, and settings that defined the scope of this HTA, which are further described in the sections that follow the table. Two review team members independently screened titles, abstracts, and full-text articles based on these study selection criteria. Discrepancies in study selection at the full-text level were adjudicated by the lead investigator, or in some cases, by team consensus.

Table 1. Population, Intervention, Comparator, Outcomes, Timing, Setting and Other Study-Selection Criteria for HTA on Non-invasive, Non-pharmacological Treatment of Tinnitus

Domain	Included	Excluded
Population	• Adults with subjective tinnitus that is bothersome (i.e., warrants treatment) • Adults whose tinnitus is described as primary, idiopathic, or neurophysiologic • Adults for whom an underlying, anatomical condition as the source of the tinnitus has already been ruled out • Adults whose tinnitus may be attributed to acoustic trauma (e.g., prolonged noise exposure, blast exposure), head and neck trauma (e.g., whiplash), traumatic brain injury (e.g., concussion), or ototoxic medication exposure that is irreversible • Adults with co-morbid hearing loss.	• Adults with subjective tinnitus that is not bothersome (i.e., does not warrant treatment) • Adults with objective tinnitus • Adults whose tinnitus is caused by an underlying, anatomical condition (e.g., tumors of the head and neck, vascular disorders, TMJ, eustachian tube dysfunction, cervical-spinal disorders, obstructions in the middle ear) • Studies conducted in adolescents, children, in animals, *in vitro*, or *in silico*
Intervention	• Sound generators/maskers • Hearing aids with specific sound generation/masking capabilities • Repetitive transcranial magnetic stimulation (rTMS)[a] • Cognitive behavioral therapy[b] • Tinnitus retraining therapy • Neuromonics tinnitus treatment • Tinnitus activities treatment	• Other non-invasive neuromodulation therapies[a] and psychological/behavioral therapies[b] not already included • Pharmacologic treatments • Supplements, herbal, and homeopathic remedies • Cochlear implantation • Invasive neuromodulation therapies[c] • Alternative and complementary medicine therapies[d]

Domain	Included	Excluded
	• Combination therapies that combine any of the included interventions, including the therapeutic components of progressive tinnitus management	• Diet, exercise, and sleep hygiene modifications • Low-level laser therapy • Progressive tinnitus management that is being studied as an implementation or delivery strategy
Comparator	• No treatment • Usual care (as defined by the study) • Waitlist or delayed treatment • Sham treatment	• All excluded interventions above • Another included intervention[e] • No comparator group
Outcomes	• **EQ**: Validated tinnitus symptom severity or handicap, depression, anxiety, sleep, health-related quality of life, functional status • **SQ**: Serious adverse events, adverse events, side effects including device-related complications • **CQ**: Cost; cost-effectiveness	• **EQ**: Outcomes related to hearing loss • **EQ**: Outcomes measured by non-validated scales
Timing & Language	• No timing restrictions • English-language articles	• No timing exclusions • Non-English-language articles
Setting	• Countries categorized as "very high human development" according to the United Nations Development Programme's 2018 Human Development Report[f,10] • Primary or specialty care (audiology, otolaryngology, neurology, mental health)	• Countries not categorized as "very high human development" according to the United Nations Development Programme's 2018 Human Development Report[f,10] • No exclusions based on care setting
Study Design	• **EQ**: RCTs, CCTs; if fewer than 3 some- or low risk of bias RCTs or CCTs are included, then cohort studies with a concurrent comparator group will also be included • **SQ:** RCTs, CCTs, cohort studies with a concurrent comparator group • **CQ**: CEA, CUA, or CBA performed from the societal or payor perspective	• Editorial, comments, or letters; conference abstracts; case reports or case series; case-control studies; other observational study designs without a comparator group not already specified • Relevant narrative or systematic reviews (or similar publications) will be hand searched to identify potentially eligible primary studies

Notes: [a] Studies of other non-invasive neuromodulation therapies are excluded, but listed in Appendix G for reference. This includes but is not limited to: transcranial direct current stimulation, neurofeedback, transcutaneous vagus nerve stimulation, and transcutaneous electrical nerve stimulation.
[b] Studies of other psychological/behavioral therapies are excluded but listed in Appendix G. This includes but is not limited to: mindfulness-based stress reduction, acceptance and commitment therapy, biofeedback, and other psychological, behavioral, or counseling therapies, including relaxation techniques.
[c] Including, but not limited to: implanted vagus nerve stimulation; deep brain stimulation; and brain surface implants.
[d] Including, but not limited to: acupuncture; hyperbaric oxygen therapy; hypnosis; manipulative and body-based approaches (e.g., chiropractic care, massage); and whole body approaches (e.g., traditional Chinese medicine, Ayurvedic medicine).
[e] Comparative-effectiveness analyses of eligible interventions are excluded but listed in Appendix G.
[f] Andorra, Argentina, Australia, Austria, Bahamas, Bahrain, Barbados, Belarus, Belgium, Brunei Darussalam, Bulgaria, Canada, Chile, Croatia, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hong Kong China (SAR), Hungary, Iceland, Ireland, Israel, Italy, Japan, Kazakhstan, Korea (Republic of), Kuwait, Latvia, Liechtenstein, Lithuania, Luxembourg, Malaysia, Malta, Montenegro, Netherlands, New Zealand, Norway, Oman, Poland, Portugal, Qatar, Romania, Russian Federation, Saudi Arabia, Singapore, Slovakia, Slovenia, Spain, Sweden, Switzerland, Taiwan (not recognized by UN but would be in the "very high" category per HDI value calculated by its government), United Arab Emirates, United Kingdom, United States, Uruguay.

Abbreviations: CBA = cost-benefit analysis; CCT = controlled clinical trial; CEA = cost-effectiveness analysis; CQ = cost question; CUA = cost-utility analysis; EQ = efficacy question; PICOTS = population, intervention, comparator, outcome, timing, and setting; RCT = randomized controlled trial; SQ = safety question.

2.3.1 Population

Studies were selected if they enrolled adults with bothersome, subjective tinnitus or tinnitus described as primary, idiopathic, or neurophysiologic. We excluded adults with objective tinnitus or subjective tinnitus that is not bothersome. Studies that included persons with or without hearing loss were eligible for selection.

2.3.2 Intervention and Comparator

We selected studies that used sound generators or maskers, hearing aids with specific sound generation capabilities, rTMS, CBT, or other interventions consisting of the combination of psychological counseling and sound therapy (e.g., tinnitus retraining). We excluded studies that used non-invasive neuromodulation other than rTMS, pharmacologic treatments, herbal or dietary supplements, cochlear implantation, invasive neuromodulation therapies, alternative and complementary medicine therapies, diet or exercise modifications, low-level laser therapy, and PTM when studied as an implementation or delivery strategy. The therapeutic components of PTM were eligible for inclusion. Eligible comparators include no treatment, usual care, waitlist (i.e., delayed treatment), or sham treatment. Ineligible comparators include all excluded interventions or no comparator group. We also excluded other eligible interventions as a comparator group because comparative effectiveness was outside the scope of this HTA.

2.3.3 Outcomes

For the efficacy research question on health outcomes, we selected studies that reported using validated measures of tinnitus symptoms, severity, distress, or, handicap. We also selected studies that reported using validated measures of depression, anxiety, sleep, health-related quality of life, and functional outcomes. We did not require any minimum time between intervention and measurement of outcomes.

For the safety research question, we selected studies that reported serious adverse events, adverse events, and side effects including device-related complications.

For the cost research question, we selected studies that reported on the costs and cost-effectiveness of tinnitus interventions.

2.3.4 Settings

Studies in any care setting were eligible. Studies that were conducted in countries with a development rating designated as *very high* by the United Nations Human Development Index in 2018 were eligible for selection because these countries (e.g., Canada, Europe, Australia, New Zealand, Japan, S. Korea, Singapore, Hong Kong and others) are like the U.S. with respect to standards of medical practice.[10] We excluded studies conducted in countries with a development rating designated as less than *very high*.

2.3.5 Study Design

We selected studies that used any of the following study designs: randomized clinical trials (RCTs), controlled clinical trials (CCTs), cost analyses, cost-benefit analyses, cost-utility analyses, and cost-effectiveness analyses. We also allowed cohort studies with a concurrent comparator group for safety outcomes. We also allowed cohort studies with a concurrent

comparator if fewer than 3 low or some risk of bias RCTs or CCTs were available for any given intervention category. Case-control studies, cross-sectional studies, case reports, editorials, comments, letters, and narrative reviews were not eligible for selection. We also did not include systematic reviews, but we did search their reference lists to identify relevant primary research studies that our search may have missed.

2.3.6 Time Period

We selected studies regardless of date of publication.

2.3.7 What Is Excluded from This HTA

This review did not include studies published in languages other than English or conducted in countries that are not very highly developed based on the United Nations Human Development Index.[10] This review also did not include studies solely focused on comparative effectiveness of various interventions. Studies with multiple intervention arms were included if an eligible control group was also included; only data from the comparisons between eligible intervention groups and eligible control groups were included in this HTA. For practical purposes, we excluded less commonly used non-invasive treatments; studies using such interventions are cataloged in ***Appendix G***.

2.4 Data Abstraction and Risk of Bias Assessment

One team member extracted relevant study data into a structured abstraction form in DistillerSR, and a senior investigator checked those data for accuracy. Two team members conducted independent risk of bias assessments on all included studies; discrepancies were resolved by discussion or review by a third reviewer. We used the Cochrane Risk of Bias (RoB 2.0) tool to assess the risk of bias for each included RCT.[11] Domains assessed with this tool include: bias arising from randomization process, bias due to deviations from intended interventions, bias due to missing outcome data, bias in measurement of the outcome, and bias in selection of the reported result. Risk of bias was assessed as "high," "some concerns," or "low" at the study level, unless different outcomes within a single study required outcome-level risk of bias ratings.

2.5 Data Synthesis and Quality of Evidence Rating

We summarized continuous outcome measures as absolute mean differences (AMDs) between treatment groups where possible. When studies did not report the AMD, we calculated it and the associated 95% confidence intervals (CI) and *P* values using OpenEpi (version 3.0) when the appropriate data were reported in the article (e.g., mean, standard deviation [SD] for each group). We summarized categorical outcomes using absolute (risk difference [RD]) and relative (risk ratio [RR]) between-group differences in proportions. For efficacy outcomes, we calculated the RD and RR and associated 95% CIs when studies did not report them, and the appropriate data were reported in the article. We also conducted statistical significance testing when authors did not report it and the data were available to do so; we considered a two-tailed *P* value of < 0.05 as statistically significant.

We qualitatively synthesized study characteristics and results for each research question by intervention category in tabular and narrative formats. We were unable to quantitatively

synthesize findings because of heterogeneity in clinical intervention type, intensity, and duration; outcome measurement and timing of followup; and study design.

We graded the certainty of the evidence for each comparison and category of outcomes using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach.[12] The lead investigator graded each body of evidence and these were reviewed by another senior investigator with discrepancies resolved through discussion. With GRADE, the certainty of evidence can be graded as *very low*, *low*, *moderate*, or *high*. ***Table 2*** defines these levels.[116] Bodies of RCT evidence begin with a *high* rating and are downgraded based on domains relating to study limitations (i.e., risk of bias), inconsistency, imprecision, indirectness, and other considerations, such as publication bias. Bodies of observational evidence begin with a *low* certainty rating and can be downgraded for the same domains as used to evaluate RCTs but can also be upgraded from *low* for other considerations (e.g., large effect, evidence of dose-response). To assess the consistency domain within GRADE, we evaluated both the consistency in the direction and magnitude of treatment effect. To assess the precision domain within GRADE, we evaluated whether optimal information size (OIS) criteria were met.[117] We downgraded bodies of evidence that did not meet OIS criteria by either 1 or 2 levels of certainty. If OIS criteria were met but the confidence intervals were either not provided or could not exclude a meaningful benefit or harm, then we downgraded for imprecision.

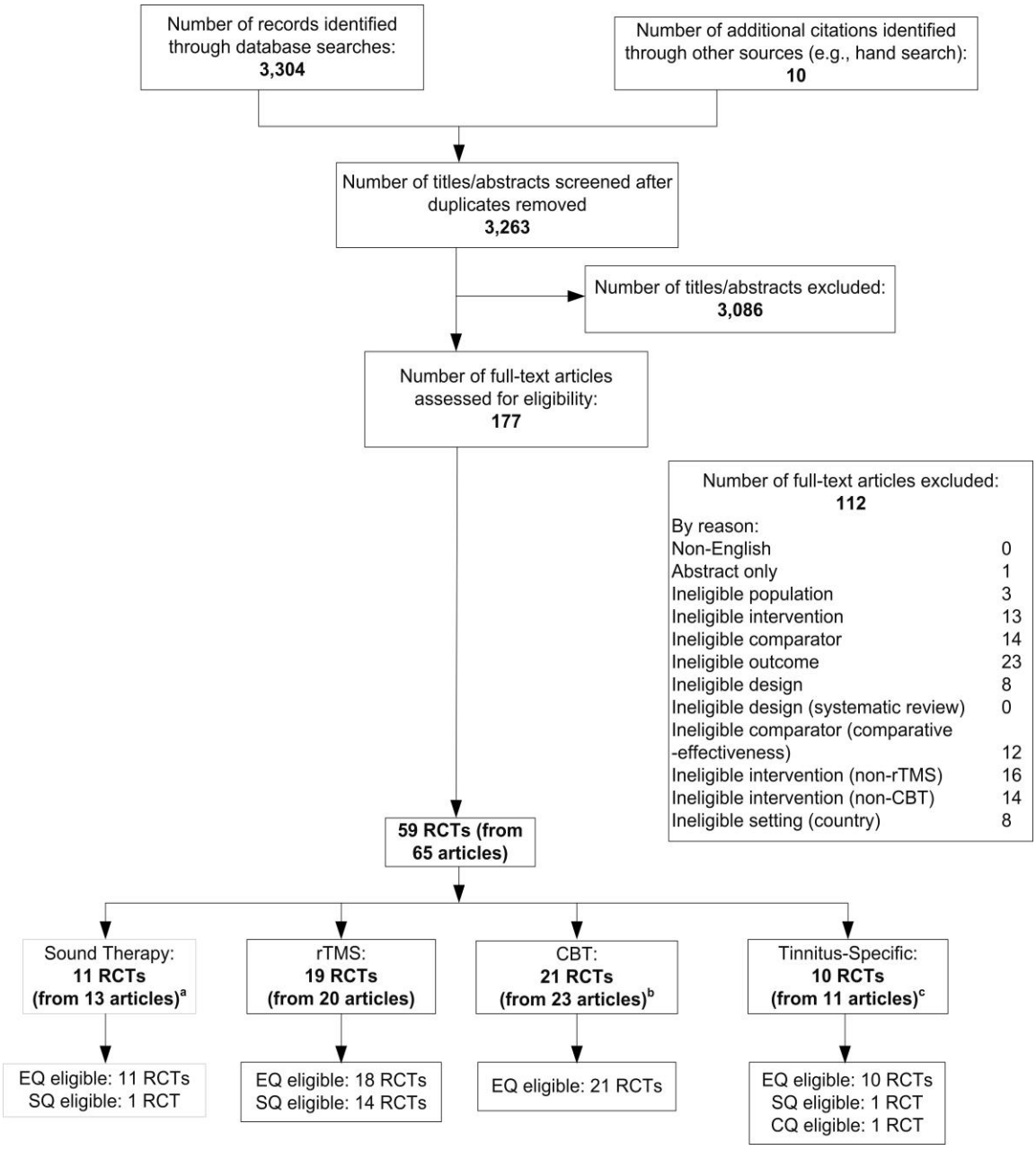
Table 2. Certainty of Evidence Grades and Definitions[116]

GRADE	Definition
High	**We are very confident that the estimate of effect lies close to the true effect for this outcome.** The body of evidence has few or no deficiencies. We believe that the findings are stable, that is, another study would not change the conclusions.
Moderate	**We are moderately confident that the estimate of effect lies close to the true effect for this outcome.** The body of evidence has some deficiencies. We believe that the findings are likely to be stable, but some doubt remains.
Low	**We have limited confidence that the estimate of effect lies close to the true effect for this outcome.** The body of evidence has major or numerous deficiencies (or both). We believe that additional evidence is needed before concluding either that the findings are stable or that the estimate of effect is close to the true effect.
Very Low	**We have very limited confidence that the estimate of effect lies close to the true effect for this outcome.** The body of evidence has numerous major deficiencies. We believe that substantial additional evidence is needed before concluding either that the findings are stable or that the estimate of effect is close to the true effect.

3. Results

Figure 2 depicts the study flow diagram. We screened 3,263 unique citations and excluded 3,086 citations after title and abstract review. We dually reviewed 177 full-text articles and included a total of 59 studies reported in 65 articles published between 1996 and 2019. Fifty-eight studies provided evidence on effectiveness (EQ 1), 16 studies provided evidence for safety outcomes (SQ 1), and 1 study provided evidence on cost outcomes (CQ 1). Individual study and population characteristics and findings are summarized in tables in ***Appendix D***. The list of articles we screened at the full-text stage, but which we excluded, is provided in ***Appendix E***. Note that articles may have been excluded for multiple reasons, but we report only one reason. We

Figure 2. Study Flow Diagram for HTA on Non-invasive, Non-pharmacologic Treatments for Tinnitus



Notes:
[a] Includes 1 study that also had a tinnitus-specific study arm.
[b] Includes 1 study that also had a CBT study arm.
[c] Includes 1 study that also had a sound therapy arm and CBT study arm.

Abbreviations: CBT = cognitive behavioral therapy; CQ = cost question; EQ = effectiveness question; rTMS = repetitive transcranial magnetic stimulation; SQ = safety question.

report our individual study risk of bias assessments for included studies in ***Appendix F***. Studies using neuromodulation or psychological therapies that were excluded as outside the scope of this review and comparative effectiveness studies are cataloged in ***Appendix G***.

The next section (Section 3.1) provides an overview of the varied measures used to evaluate the effect of treatment on tinnitus distress and disability and psychological outcomes. Following this section, the results are organized by intervention category. First, we describe findings from sound therapies (Section 3.2), then rTMS interventions (Section 3.3), then CBT interventions (Section 3.4), followed by tinnitus-specific interventions (Section 3.5). Some overlap in intervention components exists across these categories; we included studies with multiple, eligible study arms in more than 1 category for our synthesis. Further, we categorized studies into these 4 intervention groups based on what we assessed was the study's primary intervention, even if the study included additional supporting components that could also be considered in another category. We included studies with sham or delayed treatment control groups, along with studies that included attention control groups, which may have involved some form of information, education, or counseling. Attention control groups are common in behavioral intervention studies to control for the nonspecific effects of an intervention resulting from contact and social support that might be received from an intervention that is separate from the intervention's 'active ingredient'.[118] We relied on the study authors' characterization of study groups as being designed to serve as attention control groups to distinguish these groups from trials assessing 2 active interventions in a head-to-head comparison, which were outside the scope of this HTA (***Appendix G***).

3.1 Overview of Outcomes Used and Analyses Reported

3.1.1 Outcomes Used

Studies included in this review used a variety of validated instruments and scales to measure the effectiveness of tinnitus treatment across a range of outcome domains. ***Table 3*** summarizes the measures designed to measure the effect of treatment on tinnitus-related distress and disability.[13,14] One or more of these measures were used by nearly all of the included studies that designated a primary study endpoint or that powered studies based on a specific outcome. Given the subjective nature of tinnitus, most of these tinnitus-specific instruments are designed as patient-reported measures. Some instruments were primarily developed to classify the severity of a person's tinnitus-related distress or disability and secondarily have been used to evaluate the effect of treatment interventions. Other instruments were designed to both classify severity and evaluate changes in distress or disability resulting from treatment interventions. Some instruments attribute a qualitative label to specific score ranges whereas others are scored on a continuum without clear thresholds for classifying distress and disability. For most (but not all) instruments, a higher score indicates worse distress or disability. A clinically meaningful difference has been established for some, but not all measures.

Studies have found high correlation among the various measures suggesting that they measure a similar underlying construct; the differences among the measures concern resolution in measurement and variation in the distribution of items across the domains of distress and disability, including sleep, auditory perception, health, impact on lifestyle,

Table 3. Summary of Validated Tinnitus Distress and Disability Measures Reported by Included Studies.

Instrument	Description	Score Range	Directionality of Scale	Minimally Important Difference	Sensitivity for Change Due to Treatment Interventions
Tinnitus Handicap Inventory (THI)[119-123]	25 patient-reported items measuring global tinnitus severity and distress, including emotional reactions, daily functioning, and catastrophizing; items are scored as 0 (no), 2 (sometimes) or 4 points (yes).	0-100; 0-16 (no handicap), 18-36 (mild handicap), 38-56 (moderate handicap), 58-100 (severe handicap)	Higher scores reflect worse distress	6 to 7 points for improvement	Studies demonstrate sensitivity to change even though this instrument was developed primarily to stratify the severity of tinnitus.
Tinnitus Questionnaire (TQ) and derivative mini-Tinnitus Questionnaire (TQ)[121,124-127]	52 items to measure impairment due to tinnitus, includes subscales of emotional distress, cognitive distress, intrusiveness, auditory percentual difficulties, sleep disturbances, and somatic complaints. The modification used in most German studies only scores 40 of the items and counts 2 items as double. The mini-TQ includes 10 items from the larger questionnaire.	TQ: 0 10 104 (or 84 for modified version) 1-30 (low), 31-46 (moderate), 47-59 (severe), 60-84 (very severe) Mini-TQ: 0-20	Higher scores reflect worse distress	5 points for improvement 1 point for deterioration	Studies demonstrate sensitivity to change even though this instrument was developed primarily to stratify the severity of tinnitus.
Tinnitus Handicap Questionnaire (THQ)[128-130]	27 items with 3 subscales: 1) impact on social, emotional, and physical aspects, 2) hearing ability and unease, 3) individual's outlook on tinnitus. Each item is rated on a 100-point scale, with all item scores scaled to a 0-100 range.	0-100	Higher scores reflect worse distress	21 points for improvement	Developed to measure severity and to be sensitive to change over time.
Tinnitus Reaction Questionnaire (TRQ)[130,131]	26 items that use a 5-point scale to assess general distress, interference, severity, and avoidance. Some studies suggest this is the least tinnitus-specific instrument, with some overlap with more general questionnaires measuring depression and anxiety.	0-104; a score of 17 or above is considered indicative of significantly intrusive tinnitus	Higher scores reflect worse distress	Not established	Developed to measure the effects of psychological interventions on tinnitus and to distinguish levels of distress.
Tinnitus Functional Index (TFI)[132-134]	25 items covering 8 aspects of tinnitus handicap, each item measured on a scale of 0-10.	0-100, scores > = 25 indicate a significant problem with tinnitus	Higher scores reflect worse distress	13 points for improvement	Developed to provide a responsive measure to treatment-related change and to discriminate between levels of tinnitus distress.
Visual analog scales (VAS) for tinnitus loudness, annoyance, discomfort, distress, disruption, unpleasantness,	Participants are asked to rate various aspects of tinnitus distress (e.g., annoyance, loudness, severity, coping, control) on a visual analog scale. VAS varies in actual use by the length of the line used, and whether or not marks and labels are included on the line.	0-10 for scales assessed in centimeters; 0-100 for scales assessed in millimeters.	Depends on the specific attribute being assessed; higher or lower may reflect worse distress	Between 10- and 15-points (on a 100 mm scale) improvement; alternatively, a relative change	VAS is widely used as measure of patient-reported outcomes, but few studies evaluate its sensitivity to change related to treatment for chronic tinnitus. Further wide variation in its administration may result in less valid

Instrument	Description	Score Range	Directionality of Scale	Minimally Important Difference	Sensitivity for Change Due to Treatment Interventions
sleep quality, awareness, stress, control, coping[135]				of ≥30%	measurement.
Tinnitus Experience Questionnaire (TExQ)[73]	7 items assessing loudness and bothersomeness of tinnitus.	Unclear	Unclear	Unclear	Unclear
Tinnitus Effects Questionnaire (TEfQ)[124,136,137]	52 items assessing effects of tinnitus on emotions, sensory and perceptual difficulties, and sleep. Each item assessed as "true", "partly true", or "not true".	Unclear	Unclear	Unclear	Unclear
Tinnitus Cognitions Questionnaire (TCQ)[138]	26 items measuring the positive and negative thoughts associated with tinnitus; each item is rated on a 5-point scale.	0-104	Higher scores indicate worse distress	Unclear	Unclear
Tinnitus Disability Questionnaire (TDQ)[139]	Unclear	Unclear	Unclear	Unclear	Unclear
Tinnitus Coping Style Questionnaire (TCSQ)[140,141]	33 items assessing a broad range of adaptive and maladaptive coping strategies; each item rated on a 7-point Likert scale.	Unclear	Higher scores on maladaptive subscale reflect poor coping skills Higher scores on effective coping scale reflect better coping	Unclear	Unclear
Tinnitus Severity Index (TSI)[142]	12 items assessing how much tinnitus is perceived as bothersome or as negatively impacting a patient's life.	0 to 48	Unclear	Unclear	Unclear
Tinnitus Acceptance Questionnaire (TAQ)[143,144]	12 items divided into 2 subscales, activity engagement and tinnitus suppression.	0-72	Higher scores indicate higher levels of tinnitus-related acceptance	Not established	Not clear
Tinnitus Severity Scale (TSS)[145,146]	15 items designed to quantify cognitive and behavioral responses to tinnitus in the following domains: intrusiveness, distress, hearing loss, sleep disturbance, and medication.	0-39	Higher scores indicate worse symptoms	Unclear	Unclear

psychological/emotional impact, and tinnitus-specific effects. With respect to resolution for example, the Tinnitus Functional Index measures individual items on a 0 to 10 scale, which limits its resolution; further this measure includes quality of life measures, which makes it less sensitive to change from tinnitus treatment since quality of life can be impacted by many things other than tinnitus. With respect to variation in the distribution of items, 79% of items on the Tinnitus Reaction Questionnaire (TRQ) concern psychological/emotional impact whereas only 36% of items on the TFI relate to psychological/emotional impact.[147]

In addition to measures of tinnitus-related distress and disability, included studies also used various validated instruments to measure the impact of treatment on more general psychological and emotional status, sleep impact, and quality of life. *Error! Not a valid bookmark self-reference.* summarizes these measures. These measures are commonly used to assess the effect of variety of treatment interventions across many therapeutic areas beyond the treatment of tinnitus; thus, they may be less sensitive to change from tinnitus-specific interventions. Further, almost no included studies designated these measures as a primary study endpoint or powered studies based on these outcomes.

3.1.2 Analyses Reported

The studies in this body of evidence reported varied outcomes using different approaches to analysis. For purposes of this HTA, we focused our synthesis and assessment on data reported that represented the difference in outcome between the treatment intervention group and the control group (between-group difference). Some studies reported findings based on a difference-in-difference between groups at a single or multiple discrete follow-up timepoint, whereas other studies reported using repeated measures analyses, based on differences between groups at multiple timepoints over followup. Lastly some studies reported results using standardized effect size measures, rather than absolute differences in measures. Effect sizes are parameters that convey the mean difference between groups standardized by the variance associated with the means of each groups. Cohen's *d* and Hedges *g* are 2 commonly reported standardized effect size measures.[148] A standardized effect size of 1.0 indicates that the 2 groups differ by 1 standard deviation. A Cohen's *d* of 0.20 is considered a small effect, 0.50 is considered a medium effect, 0.80 is considered a large effect, and 1.20 is considered a very large effect.[149,150]

Table 4. Summary of Validated Measures of Psychological Status and Quality of Life Reported by Included Studies.

Instrument	Description	Score Range	Directionality of Scale	Minimally Important Difference	Sensitivity for Change Due to Treatment Interventions
Anxiety and Depression					
Hospital Anxiety and Depression Scale (HADS)[151,152]	14 items resulting in a depression subscore (7 items) and an anxiety subscore (7 items); each item is scored on a scale of 0-3.	0-21 for each subscore; 0-7 normal, 8-10 is borderline, and 11-21 is abnormal	Higher scores indicate worse depression or anxiety	1.7 points	Developed initially for screening/ detection; unclear whether sensitive to changes from tinnitus treatment.
Beck Depression Inventory (BDI-II)[153-155]	21 items measuring characteristic attitudes and symptoms of depression.	0-63; 0-13 minimal depression; 14-19 mild depression; 20-28 moderate depression; 29-63 severe depression	Higher scores indicate worse depression	5 points or 17.5%-30% reduction in score	Validated measure for assessing response to treatment.
Hamilton Rating Scale for Anxiety (HAM-A)[156]	14 items, each scored on a scale of 0 (not present) to 4 (severe)assessing the severity of symptoms of anxiety.	0-56; <17 mild severity; 18-24 mild to moderate severity; 25-30 moderate to severe	Higher scores indicate worse anxiety	Unclear	Unclear
Hamilton Rating Scale for Depression (HAM-D)[157,158]	21 items, scoring based on the first 17 items; items are scores on a 5-point scale.	0-7 normal; 8-13 mild; 14-18; moderate, 19-22 severe ; ≥ 23 very severe depression	Higher scores indicate worse depression	2-3 points or 27%-28% reduction	Validated for response to treatment
Allgemeine Depression Scale (ADS)[159]	German version of the Center for Epidemiological Studies measuring general depression	0-60; >23 indicates a depressive disorder	Higher scores indicate worse depression	Unclear	Unclear
Anxiety Sensitivity Index (ASI)[160]	16-item scale intended to specify a possible negative consequence to the experience of anxiety. Each item is assigned a phrase corresponding to a point of value.	0-64; 0 (very little); 1 (a little); 2 (some); 3 (much); 4 (very much)	Higher scores indicate worse anxiety	Unclear	Unclear
Depression, Anxiety, and Stress Scales (DASS)[161,162]	A set of three, 14-item self-report scales (42 items total), divided into subscales of 2-5 similar items, designed to measure the negative emotional states of depression, anxiety, and stress, respectively. Subjects use 4-point severity/frequency scales to rate the degree to which they have experienced each state in the past week.	0 (did not apply); 1 (applied to some degree, or some time); 2 (applied a considerable degree, or a good part of the time); 3 (applied very much, or most of the time)	Higher scores indicate worse depression, anxiety, and/or stress	Unclear	Unclear
Generalized Anxiety Disorder, 7-item Scale (GAD-7)[163,164]	Subjects are asked how often in the past two weeks they were bothered by each of the 7 items on the scale (which comprise the 7 symptoms of generalized anxiety disorder).	0-21; 0 (not at all); 1 (several days); 2 (more than half the days); 3 (nearly every day)	Higher score indicates worsening of anxiety	Unclear	Validated measure for assessing response to

Instrument	Description	Score Range	Directionality of Scale	Minimally Important Difference	Sensitivity for Change Due to Treatment Interventions
		≥5 mild; ≥10 moderate; ≥15 severe			treatment
General Mental Health and Well-being					
Symptom Checklist-90-Revised (SCL-90R)[165,166]	90 items to evaluate a broad range of psychological symptoms broken into 9 primary symptoms (somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid Ideation, psychoticism	Reports normed subscores for each of the 9 scales along with a global severity index	Scores are reported normed to population	Unclear	Unclear
General Health Questionnaire (GHQ-12)[167]	12 items assessing for psychological disorders in primary health care and outpatient settings; produces 3 subscores, anxiety and depression, social dysfunction, and loss of confidence	12-36	Higher scores indicate higher clinical severity	Unclear	Unclear
Perceived Stress Scale[168-170]	10-item measure of perceived stress, each item is rated on a scale of 0-4.	0-40; 0-13 low stress, 14-26 moderate stress, 27-40 high stress	Higher scores indicate worse stress	11 points or 28% reduction in score	Unclear
Derogatis Stress Profile[171,172]	77-item inventory assessing 11 dimensions of environment, personality mediators, and emotional response; each item is rated on a 5-point scale	Scores are normed	Higher scores indicate worse stress	Unclear	Unclear
Perceived Stress Questionnaire[173]	20 items with 4 subscales (worry, tension, joy, and demands)	0-100; scores less than 49 indicate a low stress level	Higher scores indicate more stress	Unclear	Unclear
Coping Inventory (COPE)[174]	20-item assessment of five domains of coping; each item assessed with a 4-point scale.	Each domain can range from 4 to 16.	Varies by domain	Unclear	Unclear
Ways of Coping Check List Revised (WCCL-R)[175,176]	66-item assessment; each item is assessed on a 4-point scale; produces subscores for 8 domains	Unclear	Unclear	Unclear	Unclear
Sleep					
Insomnia Severity Index (ISI)[177,178]	7 items assessing problems related to sleep, insomnia, sleep quality, negative impact of sleep loss on daily functioning, each item is scored 0-4	0-28, 0-7 no clinically significant insomnia, 8-14 subthreshold insomnia, 15-21 moderate clinical insomnia, 22-28 severe clinical insomnia	Higher scores indicate worse insomnia	6- to 7-point reduction	Unclear
Epworth Sleepiness Scale(ESS)[179,180]	8-item assessment for screening for sleep disorders, measures excessive daytime sleepiness; each item scored on a 4-point scale.	0-24; 0-10 normal, 11-12 (mild), 13-15 (moderate), 16-24 (severe)	Higher scores indicate a higher chance of dozing in everyday circumstances.	Unclear	Has been demonstrated to be responsive to changes from treatment

Instrument	Description	Score Range	Directionality of Scale	Minimally Important Difference	Sensitivity for Change Due to Treatment Interventions
Jenkins Sleep Evaluation Questionnaire (JSEQ)[181]	4-item questionnaire assessing sleep problems experienced in the past month, with six response categories possible for each item, coded on a scale of 0-5.	0-20; 0 (not at all); 1 (1-3 days); 2 (4-7 days); 3 (8-14 days); 4 (15-21 days); 5 (22-31 days)	Higher scores indicate higher degree of sleep problems	Unclear	Unclear
Quality of life					
World Health Organization Quality of Life Assessment -Brief Version (WHOQoL-BREF)[182]	26 items producing scores in 4 domains: physical health, psychological, social relationships, and environment in addition to overall quality of life and general health	0-100	Higher scores indicate a higher QoL	Unclear	As a generic instrument, may be less responsive to treatment for specific conditions.
Quality of Life Inventory[183]	Measures QoL in 16 domains each scored on two scales, one for importance and one for satisfaction	Scores are normed	Higher scores indicate higher QoL	Unclear	Unclear
Short Form Survey Physical Health Component Score (SF-36 PCS)[184,185]	36-item assessment; 4 of the 8 domains are combined to produce a health-related QoL measure related to physical health	Scores are normed, 0-100	Higher scores indicate a higher QoL	2.5- to 5-point increase	Unclear
Short From Survey Mental Health Component Score (SF-36 MCS)[184,185]	36-item assessment; 4 of the 8 domains are combined to produce a health-related QoL measure related to mental health	Scores are normed, 0-100	Higher scores indicate a higher QoL	2.5- to 5-point increase	Unclear
Health Utilities Index (HUI) Mark 3[186]	17-item questionnaire designed to assess health-related QoL or generic health on 8 dimensions (vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain or complaints). Each question has 5-6 levels of response.	Using a multi-attribute utility function: minimum -0.36 (most disabled); 0.00 dead; maximum 1.00 (perfect health)	Higher score indicates increasing health or QoL	Unclear	Unclear
Global improvement					
Clinical Global Impression Scale-Improvement (CGI)[187]	Structured interview measuring the patients experienced change in response to treatment; the improvement scale is on 7-point scale	1 (very much improved) to 7 (very much worse) 3 (minimally improved); 4 (no change); 5 (minimally worse)	Higher scores indicate worsening of condition.	Unclear	Unclear

Abbreviations: QoL = quality of life.

3.2 Sound Therapy Interventions

We identified 11 RCTS described in 13 publications that focused on sound therapy.[15-25] These studies evaluated the following 4 comparisons: 1) hearing aids with sound generating features compared to standard hearing aids, 2) altered auditory stimulus compared to sham stimulus, 3) sound generators with counseling, education, or information compared to those interventions without sound generators, and 4) an auditory attention training game compared to a sham training game. One of the studies[24] included in this section also featured an eligible tinnitus-specific intervention in addition to the sound therapy intervention; the results from the tinnitus-specific intervention are detailed in the tinnitus-specific therapies section of this report (Section 3.5). Key findings are:

- Eleven RCTs[15-24,188] reported measures of tinnitus distress or disability, which were the primary outcomes in most trials. Most studies reported no significant differences between intervention and control groups; however, altered studies involving auditory stimulus interventions observed mixed findings. Among the 4 studies evaluating this type of intervention, 2 studies reported a statistically significant difference in measures of tinnitus distress or disability, favoring the intervention, whereas 2 observed no statistically significant differences.
- Two RCTs[17,19] reported on psychological measures. No statistically significant differences were measured between intervention and control groups in either of the 2 trials.
- One RCT[20] reported adverse events, which were not significantly different between the intervention group and control group.
- No RCT reported on cost outcomes.

The rest of this section provides detailed study and population characteristics and results.

3.2.1 Study and Population Characteristics

The included sound therapy trials were conducted from 1999 to 2018. We assessed 5 RCTs as having some risk of bias,[16,20,21,23,188] and 6 RCTs as high risk of bias.[15,17-19,22,24] Three trials[15,16,188] were conducted in the United States,[15,16,188] 4 trials[20-23] in Germany, 2 trials[19,24] in Australia, and 1 trial each in Canada[17] and New Zealand.[18] Industry funding was provided partially or in full for approximately half of the included studies, whereas the other half did not receive or report receiving industry support. ***Table 5*** includes the characteristics of included sound therapy RCTs, with additional details found in ***Appendix D, Tables D1a, D1b,*** and ***D1c.***

Of the included studies, the sample sizes ranged from 30 to 136 patients. However, 8 RCTs[15-19,21,22,189] had sample sizes of less than 50 patients. The mean age of included populations ranged from 41 to 67 years. Ten of the 11 studies included both male and female participants; the percentage of female participants ranged from 20% to 58%. Only 1 study[189] provided data about participant race, which was 90% white. Patients with some degree of hearing loss were included in 7 studies,[16,18-20,23,24,189] whereas 3 studies excluded participants with hearing loss[15,17,83]; 1 study did not report information about participant's hearing loss.[21,22] Most studies that used hearing aids as part of a sound therapy intervention required that patients met the hearing loss thresholds

required for use of such devices. Patients with blast injury were included in 1 study,[23] whereas the remaining studies did not report blast injury as part of the participant characteristics.

Table 5. Summary of Study Characteristics of Included Studies of Sound Therapies for the Treatment of Tinnitus

Author (Year)	Country	Risk of Bias	Eligible Interventions & Comparators (N randomized)	Total Sample Size[a]	Treatment Duration	Mean Age (SD)	N (%) Female	Outcomes Reported
Davis (2008)[24]	Australia	High	Counseling only (13) Acoustic stimulus plus counseling (15)	28	1 year	49.8 (15.8)	24 (48.0*)	Tinnitus distress
Dineen (1999)[19] Dineen (1997)[25] Dineen (1997)[190]	Australia	High	Information only (28) Information with sound device (20)	48	NR	53.6 (15.0)#	28# (58.3*)	• Tinnitus distress • Psychological
Henry (2015)[189]	U.S.	Some	Hearing aid only (15) Hearing aid with sound generator (15)	30	3-4 months	67.2 (9.2)	10* (33)	Tinnitus distress
Henry (2017)[16]	U.S.	Some	Hearing aid only (18) Hearing aid with sound generator (19)	37	4-5 months	Mean (Range) Hearing aid: 61 (48-75) Hearing aid+sound: 64 (54-75)	Hearing aid: 4 (22) Hearing aid+sound: 4 (21)	Tinnitus distress
Hiller (2005)[23]	Germany	Some	Tinnitus education without sound generator (36) CBT without sound generator (33) Tinnitus education plus sound generator (34) CBT plus sound generator (33)	136	Education: 4 weeks Education or CBT+ sound: 10 weeks	Education: 45.2 (14.1) Education+sound: 52.5 (15.3) CBT+sound: 51.0 (13.2)	Education: 13* (39) Education+sound: 15* (48) CBT+sound: 10* (32)	Tinnitus distress
Li (2016)[17]	Canada	High	Placebo music (25) Altered music (25)	50	1 year	Placebo: 55.8 (8.5) Altered: 55.2 (13.9)	Control: 10* (40)* Altered: 6* (24)*	• Tinnitus distress • Psychological
Okamoto (2010)[22]	Germany	High	Placebo music (13) Notched music (13)	26	1 year	40.5 (10.8)	NR	Tinnitus distress
Schad (2018)[15]	U.S.	High	Placebo noise (10) Notched noise (10) Matched noise (10)	30	2 weeks	58 (NR)	10 (33*)	Tinnitus distress
Stein (2016)[20]	Germany	Some	Placebo music (50) Notched music (50)	100	3 months	47.5 (10.8)	33* (33)	• Tinnitus distress • Safety
Strauss (2015)[21]	Germany	Some	Hearing aid (10) Hearing aid plus sound generator (10)	20	3 weeks	Hearing aid: 53.5 (4.8) Hearing aid+sound: 52.7 (5.9)	Hearing aid: 1 (10*) Hearing aid+sound: 2 (20*)	Tinnitus distress

Author (Year)	Country	Risk of Bias	Eligible Interventions & Comparators (N randomized)	Total Sample Size[a]	Treatment Duration	Mean Age (SD)	N (%) Female	Outcomes Reported
Wise (2016)[18]	New Zealand	High	Control computer game (16) Attention training computer game (15)	31	20 days	Control: 62.3 (4.6)# Attention training: 52.3 (10.6)#	10 (32.3*)#	Tinnitus distress

Notes: * Indicates a data value that we calculated based on data provided in the publication. # Indicates that the data was only reported for study completers, not the number that was randomized. [a] From study arms eligible for inclusion in this HTA.

Abbreviations: CBT = cognitive behavioral therapy; NR = not reported; SD = standard deviation; U.S. = United States.

Three studies compared hearing aids with sound-generating capabilities to control groups using hearing aids without sound-generating capabilities.[16,21,189] Four studies consisted of interventions that incorporated some form of altered auditory stimulus (e.g. notched/altered music) that participants were instructed to listen to, typically with headphones for between 1 and 6 hours per day compared to placebo auditory stimulus (i.e., unaltered music).[15,17,20,22] Three studies compared a sound generator with CBT, other counseling, or information alone to counseling, CBT, or information alone.[19,23,24] Lastly, 1 study compared an auditory attention training computer game to a control computer game.[18] Three trials were conducted over less than 1 month,[15,18,21] 4 trials were conducted over 1 to 6 months,[16,20,23,189] and 3 trials were conducted over 1 year[17,22,24]; duration was not reported for 1 study.[19] Study authors reported levels of adherence to the sound therapy interventions in 6 studies[15,20,22-24,189]; adherence was not reported in 5 studies.[16-19,21]

3.2.2 Findings

Detailed findings from studies evaluating sound therapies are provided in ***Appendix D, Tables D1d*** and ***D1e.***

3.2.2.1 Hearing Aid Interventions

Three RCTs compared hearing aids (HAs) to hearing aids with sound-generating (HA+SG) capabilities and only reported tinnitus-related disability or distress measures.[16,21,189]

Tinnitus-Related Disability and Distress

Two RCTs[16,189] reported using the TFI and 1 RCT[21] reported using the 12-question Mini Tinnitus Questionnaire (Mini-TQ). Both studies that used the TFI reported no statistically significant difference in mean change in TFI score at the end of the intervention (3 to 5 months) between the HA and HA+SG groups. The difference in TFI score improvements was 12.5 ($P = 0.079$)[16] and 6.4 points (*P* NR and unable to be calculated).[189] The majority of participants in both the HA and HA+SG groups reported a clinically meaningful TFI improvement (i.e., reduction of 13 points or more); however, the difference in proportion between groups was not statistically significantly different in either study ($P = 0.21$ and $P = 0.99$). The study that used the Mini-TQ did not report numeric outcome data but indicated overlapping confidence intervals for the difference in mean score between the HA and HA+SG groups at 3 weeks (effect size 0.84 [considered large]; 95% CI, NR).

3.2.2.2 Altered Auditory Stimulus Interventions

Four RCTs compared auditory stimulus interventions (altered frequency music or noise) to placebo auditory stimulus interventions.[15,17,20,22] None of the studies reported quality of life or cost outcomes.

Tinnitus-Related Disability and Distress

Several different tinnitus-related disability and distress measures were used in this body of evidence including various visual analog scale (VAS) assessments, the TFI, the Tinnitus Handicap Inventory (THI), and the Tinnitus Handicap Questionnaire (THQ).

Two studies used the TFI to measure outcomes.[15,17] One study compared altered notched music and matched music to unaltered music (placebo control) and reported outcomes at 2 and 4 weeks[17] whereas the other compared notched frequency noise to low-frequency noise (placebo control) and reported outcomes at 3 and 6 months and at 1 year.[15] The intervention groups in both studies reported numerically greater improvement in scores across all timepoints (between-group differences, range: -7.8 to -1.9 cm); however, the differences between intervention and placebo groups were not statistically significantly different except for 1 timepoint (6 months) in 1 study.[17] In this study, the THI was the designated primary study outcome and study authors reported a statistically significant difference in improvement on the THI score in the altered music group compared to the control music group across 3 measured timepoints (-12.8 points, *P* = 0.0008 at 3 months; -14.9 points , *P* = 0.0001 at 6 months; -17.4 points at 1 year).[17] The other study reported a VAS assessment for tinnitus loudness in addition to the TFI and reported no statistically significant differences at 2 or 4 weeks.[15]

The other 2 studies using altered auditory stimuli reported using a VAS assessment. One study reported a VAS assessment for tinnitus loudness[22] and 1 study used a VAS total score, which averaged VAS assessments of loudness, annoyance, awareness and handicap.[20] Results from these studies were mixed. One study did not report numeric data but found that the notched music group had a statistically significant improvement compared to the placebo music group over 7 to 12 months (*P* = 0.03).[22] The other study that compared tailor-made notched music to unaltered music (placebo control) reported no significant difference in total VAS score at the end of treatment (3 months) or 1 month after treatment concluded.[20] This same study also reported no significant difference between groups in THQ score at either timepoint.[20] Both outcomes (THQ and VAS total score) were designated as primary study outcomes in this study.

Psychological Measures

The only study that reported psychological outcomes used the Hospital Anxiety and Depression Scale (HADS).[17] This study compared altered music to unaltered music (placebo control) and the duration of the study was 1 year. The study authors reported no statistically significant differences between the intervention and control groups on change in the HADS-Depression (HADS-D) subscale at 6 months or 1 year, or in the HADS-Anxiety (HADS-A) subscale at 1 year. However, the authors found a statistically significant improvement in the HADS-A (2.7-point larger reduction in score) between-groups at 6 months, favoring the intervention group (*P* = 0.013).

Safety Outcomes

One study reported safety outcomes.[20] This study, which compared tailor-made notched music to unaltered music (placebo control), defined safety outcomes as additional tinnitus sounds; loudness and awareness of tinnitus sounds; and other psychological stress or bodily changes. These outcomes occurred more often in the placebo control group than in the music training group (30% versus 24%, respectively, calculated *P* = 0.51).

3.2.2.3 Sound Generation Interventions

Three RCTs compared sound generators in combination with CBT, other counseling, or information alone, to those interventions without sound generators.[19,23,24] No studies reported quality of life, safety, or cost outcomes.

Tinnitus-Related Disability and Distress

All 3 studies used a VAS assessment of tinnitus loudness and various other VAS assessments (severity, relaxation, control, unpleasantness, annoyance, and coping). All studies additionally used some form of Tinnitus distress outcome measure, including the TRQ or TQ.

In the 2 studies that reported both VAS loudness and the TRQ, follow-up scores were not significantly different between intervention and control groups at any of the follow-up timepoints measured, which included 1 year in 1 study that compared a broadband sound generator with CBT to CBT alone[24] and at 3 and 6 months in 1 study that compared a broadband noise generator plus information to information alone.[19] In the third study, which compared behind-the-ear broadband noise generators plus either education (for participants with mild tinnitus) or CBT (for participants with moderate or severe tinnitus) to education or CBT alone, the change in VAS loudness was not significantly different between the CBT with sound and the CBT-alone groups immediately following treatment or at 6 months. The change in VAS loudness was also not statistically significantly different between the education plus sound compared to the education-alone groups immediately after treatment, but the control group had a significantly larger improvement at 6 months ($P<0.05$).[23] In this same study, the TQ was also reported and no significant differences between either intervention group and the control group were observed immediately after treatment or at 6 or 18 months.

All 3 studies also reported various other VAS assessments. Changes in the VAS control and unpleasantness scores immediately after treatment and at 6 months were not statistically significantly different between groups in the study comparing sound plus education (or CBT) to education (or CBT) alone (P reported as NS).[23] Changes in the VAS severity and VAS relaxation scores were also not statistically different between the sound plus CBT group and the CBT alone group in repeated measures over the course of 1 year ($P = 0.884$, and $P = 0.696$, respectively).[24] Statistically nonsignificant findings were also reported for the VAS annoyance and VAS coping scores at 3 months and 1 year in the study comparing broadband noise generator plus information to information alone ($P = 0.83$ for annoyance and 0.17 for coping at 3 months and 0.52 and 0.52 at 1 year, for the same measures, respectively).[19]

Psychological Measures

One study that compared broadband noise plus informational materials to informational materials alone reported on psychological measures.[19] The duration of the intervention was not reported but at 12 months, no statistically significant differences were observed between groups on the Ways of Coping Checklist (WCCL-R) emotion or problem-focused subscales or on the Derogatis Stress Profile (DSP).

3.2.2.4 Attention Training Computer Game Intervention

One study compared an auditory attention training computer game ("Terrain") to a control computer game (Tetris®) and reported findings at 3 weeks post-intervention.[18] No psychological, quality of life, safety, or cost outcomes were reported.

Tinnitus-Related Disability and Distress

This study reported outcomes using the THI, TFI, and Tinnitus Severity Scale (TSS) but numeric differences were not reported for any of the outcomes. Participants in the Terrain group had a statistically significant larger improvement in THI score ($P < 0.01$) compared to the Tetris group.[18] The authors reported no statistically significant difference in the mean TFI score between groups ($P = 0.072$); however, 60% of Terrain participants improved by more than 13 points on the TFI compared to 25% of participants in the Tetris group (calculated RD = 35% [95% CI, 2.4% to 67.3%]; reported $P = 0.06$).[18] Lastly, the authors reported a statistically significant larger improvement in the TSS "ability to ignore tinnitus" scale in the Terrain group compared to the Tetris group ($P<0.01$). All other TSS scales (annoying, unpleasant, uncomfortable, and loudness) were not statistically different between groups.

3.3 Repetitive Transcranial Magnetic Stimulation Interventions

We identified 10 parallel-assignment RCTs[26-35] and 9 crossover RCTs[36-44] in 19 publications that focused on rTMS stimulation interventions compared to sham stimulation. These interventions varied in terms of the number of sessions used, the duration over which the sessions were provided, and the timing of outcome measure follow-up. Key findings are:

- Eighteen RCTs[26-36,38-44] reported measures of tinnitus distress or disability, which were the primary study aims in most studies. Most studies demonstrated no statistically significant differences in measures of tinnitus distress and disability between active rTMS and sham rTMS.
- Five RCTs[30,32,34,39,41] reported psychological measures. All studies demonstrated no statistically significant differences between active rTMS and sham rTMS in depression, anxiety, or sleep outcomes.
- One RCT[32] reported on quality of life and reported no difference between active rTMS and sham rTMS.
- Fourteen RCTs[26,28-34,36-41] reported on adverse events. Five studies reported no adverse events in either the active rTMS or sham rTMS groups, and 3 studies reported some adverse events but did not report by group. Of the remaining 6 studies, 3 reported a similar incidence of adverse events between groups, 2 reported a higher incidence of events among the active rTMS group, and 1 reported a higher incidence among the sham rTMS group.
- No RCT reported cost outcomes.

The rest of this section provides detailed study characteristics and results.

3.3.1 Study and Population Characteristics

The included rTMS trials were conducted from 2007 to 2018. We assessed 1 of these trials as low risk of bias,[32] 13 as having some risk of bias,[28-31,33-37,39-41,43] and 5 as high risk of bias.[26,27,38,42,44]

Four trials[29,37-39] were conducted in the United States, 5 trials[32,33,35,36,40] in Germany, 3 trials[42-44] in Belgium, 2 trials[26,30] in Czech Republic, and 1 trial each in Australia,[27] Finland,[34] Netherlands,[31] Taiwan,[28] and Italy.[41] Fourteen studies reported no industry support; the rest of the studies did not disclose source of funding. ***Table 6*** summarizes the characteristics of included rTMS trials, with additional details found in ***Appendix D***, ***Tables D2a, D2b,*** and ***D2c.***

Of the included studies, the eligible study sample sizes ranged from 6 to 153 participants; over half (n = 10) enrolled fewer than 30 participants. The mean age of included populations ranged from 42 to 63 years. All studies included both male and female participants; the percentage of female participants ranged from 18% to 50%. Only 2 studies[38,39] provided data about participant race, of which 79% and 93% of the sample were white, respectively. Participants with some degree of hearing loss, were included in 14 studies[27-31,33-35,37-42] whereas 3 studies excluded participants with hearing loss,[26,32,36] and 2 studies did not report information about participant's hearing loss.[43,44] Participants with blast injury were included in 1 study,[41] 2 studies excluded participants with blast injury,[33,37] whereas the remaining studies did not report whether participants with blast injury were included or excluded from study enrollment. Mean tinnitus duration among included populations ranged from 2 to 14 years.

The active intervention in all RCTs was rTMS, but studies reported variations in the rTMS protocol used. For example, 3 trials were conducted over 1 session,[42-44] 5 trials were conducted over a week or less,[30,31,36,37,41] and 11 trials were conducted from 10 days to 4 weeks.[26-29,32-35,38-40] Studies also varied in the number of pulses administered during a single session, in the frequency used, and in the stimulation intensity used. All studies included a sham rTMS control. In the parallel-assignment RCTs, the sham intervention was conducted with a sham stimulation coil; by orienting the active stimulation coil such that it was tilted away from the skull by 45 degrees; by use of a metal blocking plate; or by placing the coil at a distance that effectively lowered the level of stimulation to negligible amounts. In the crossover trials, participants served as their own controls. In 7 of the 9 crossover trials, participants were randomly allocated to receive either sham or active rTMS during the first treatment period, and received the respective other treatment (sham or active) during the second treatment period.[36-42] In the other 2 crossover trials, all participants received active rTMS during the first treatment period, followed by sham treatment in the second treatment period.[39,43] The study authors reported levels of adherence to the rTMS interventions in 12 studies[26,27,29,31-34,36,38,39,41,42]; in all but 1 trial[38] adherence was high.

Table 6. Summary of Study Characteristics of Included Studies of Repetitive Transcranial Magnetic Stimulation for the Treatment of Tinnitus

Author (Year)	Country	Risk of Bias	Eligible Interventions & Comparators (N randomized)	Total Sample Size[1]	Treatment Duration	Mean Age (SD)	N (%) Female	Outcomes Reported
Anders (2010)[26]	Czech Republic	High	Sham rTMS (26) rTMS (26)	52	2 weeks	Sham: 50.1 (14.0) rTMS: 48.1 (14.9)	13 (31)	• Tinnitus distress • Safety
Barwood (2013)[27]	Australia	High	Sham rTMS (4) rTMS (4)	8	10 days	42.4 (8.8*)	4 (50)	Tinnitus distress
Chung (2012)[28]	Taiwan	Some	Sham rTMS (10) rTMS (12)	22	10 days	53.0 (16.8)	2 (9)	• Tinnitus distress • Safety
Folmer (2015)[29]	U.S.	Some	Sham rTMS (35) rTMS (35)	70	2 weeks	Sham: 62.8 (8.3) rTMS: 58.3 (9.5)	13 (20)	• Tinnitus distress Safety
Formanek (2018)[30]	Czech Republic	Some	Sham rTMS (12) rTMS (20)	22	5 days	Sham: 51.8 (10.3) rTMS: 47.9 (14.3)	9 (28)	• Tinnitus distress • Psychological • Safety
Hoekstra (2013)[31]	The Nether-lands	Some	Sham rTMS (24) rTMS (26)	52	5 days	52 (12)	9 (18)	• Tinnitus distress Safety
Kleinjung (2005)[36] Langguth (2007)[191]	Germany	Some	Sham rTMS (10) rTMS (10)	10	5 days	47.6 (13.4)	2 (20)	• Tinnitus distress • Safety
Landgrebe (2017)[32]	Germany	Low	Sham rTMS (75) rTMS (71)	153	2 weeks	Sham: 49.9 (13.2) rTMS: 48.1 (12.5)	41 (28)	• Tinnitus distress • Psychological • QoL • Safety
Mennemeier (2011)[37]	U.S.	Some	Sham rTMS (21) rTMS (21)	21	1 week	NR	NR	• Tinnitus distress • Psychological • Safety
Piccirillo (2013)[38]	U.S.	High	Sham rTMS (20) rTMS (20)	20	4 weeks	Median 42 (range 22 to 59)	5 (36)	• Tinnitus distress • Safety
Piccirillo (2011)[39]	U.S.	Some	Sham rTMS (14) rTMS (14)	14	2 weeks	Median 52	4 (29)	• Tinnitus distress • Safety
Plewnia	Germany	Some	Sham rTMS (16)	48	4 weeks	Sham rTMS: 45.6 (10.3)	23* (48)*	• Tinnitus distress

[1] From study arms eligible for inclusion in this HTA.

Author (Year)	Country	Risk of Bias	Eligible Interventions & Comparators (N randomized)	Total Sample Size[1]	Treatment Duration	Mean Age (SD)	N (%) Female	Outcomes Reported
(2012)[33]			Secondary auditory cortex rTMS (16) Temporoparietal association cortex rTMS (16)			Secondary auditory cortex rTMS: 46.4 (13.0) Tempoparietal association cortex rTMS: 55.8 (9.7)		• Safety
Plewnia (2007)[40]	Germany	Some	Sham rTMS (6) rTMS (6)	6	2 weeks	57.7* (5.9*)	1 (17*)	• Tinnitus distress • Safety
Rossi (2007)[41]	Italy	Some	Sham rTMS (16) rTMS 1 Hz (16)	16	1 week	52.5 (10.6)	3 (21)	• Tinnitus distress • Psychological • Safety
Sahlsten (2017)[34]	Finland	Some	Sham rTMS (20) rTMS (22)	42	10 days	Sham: 51.5 (10.7) rTMS: 48.9 (13.1)	12 (31)#	• Tinnitus distress • Psychological • Safety
Schecklmann (2016)[35]	Germany	Some	Sham cTBS (11) cTBS (12)	23	10 days	Sham: 46.5 (11.5) cTBS: 48.2 (10.7)	9 (39)	Tinnitus distress
Vanneste (2012)[42]	Belgium	High	Study 1 Sham rTMS (21) Study 1 rTMS 1-Hz (21) Study 2 Sham rTMS-10 Hz (39) Study 2 rTMS 10 Hz (39)	60	1 session	50.1 (11.8)	24 (40*)	Tinnitus distress
Vanneste (2012)[43]	Belgium	Some	Study 1 Sham rTMS (24) Study 1 rTMS 1-Hz (24) Study 1 rTMS 10-Hz (24) Study 2 Sham rTMS (40) Study 2 rTMS 1-Hz (40) Study 2 rTMS 5-Hz (40) Study 2 rTMS 10-Hz (40)	64	1 session	Study 1: 52.2 (9.8) Study 2: 53.7 (7.6)	Study 1: 11 (46)* Study 2: 16 (40)*	Tinnitus distress
Vanneste (2011)[44]	Belgium	High	Sham rTMS (78) rTMS 1-Hz (78) rTMS 3-Hz (78) rTMS 5-Hz (78) rTMS 10-Hz (78 rTMS 20-Hz (78)	78	1 session	53.5 (11.9)	15 (19)*	Tinnitus distress

Notes: * Indicates a data value that we calculated based on data provided in the publication. # Indicates that the data were only reported for study completers, not the number that was randomized.

Abbreviations: Hz = electromagnetic wave frequency of stimulation; SD = standard deviation; wks = weeks; rTMS = repetitive transcranial magnetic stimulation; cTBS = continuous theta burst rTMS stimulation; QoL = Quality of life.

3.3.2 Findings

Detailed findings are provided in ***Appendix D, Tables D2d*** and ***D2e***. Most studies show no statistically significant difference in tinnitus measures of distress, QoL, and psychological measures between active rTMS and sham rTMS. Mixed findings were demonstrated across studies with regards to safety outcomes. No studies reported cost outcomes. The following section provides detailed results for each category of outcome measure.

3.3.2.1 Tinnitus Distress/Disability Measures

Ten RCTs[26-28,30-32,34,35,38,39] reported using the THI at timepoints immediately after treatment through 6 months after intervention. This measure was the primary study endpoint in most of the studies. In the studies that either reported the between-group difference in change in mean score or for which we could calculate it, the difference in change scores ranged from a 4-point larger improvement for sham rTMS to an 8.3-point larger improvement for active rTMS. Eight of the 10 studies demonstrated no statistically significant difference in THI scores between active rTMS and sham rTMS.[26,30-32,34,35,38,39] Two studies with relatively short follow-up periods of 1 week demonstrated statistically significant improvements in THI for active rTMS relative to sham rTMS ($P < 0.05$ and $P < 0.01$).[27,28] However, 1 of these studies also reported scores at 1 month with differences being no longer statistically significant.[28] In addition to changes in mean THI score, 2 of these studies also reported on the proportion of participants that experienced a clinically meaningful improvement in THI score (> = 6 or > = 11 points reduction); both reported no statistically significant difference in this proportion between active and sham rTMS groups.[31,34]

In addition to the THI, 6 studies reported on additional measures of tinnitus distress or disability including the TQ and various VAS assessments for loudness, intensity, severity, and distress.[26,28,31,32,34,35] Findings on these additional measures were consistent with findings from the THI. Four RCTs reported using VAS assessments; 3 reported a VAS assessment for loudness[42-44] and 1 reported used a VAS assessment of tinnitus discomfort.[41] These VAS assessments were the primary study aim in all 4 studies. The mean difference in change in VAS loudness scores ranged from a 0.4-point larger improvement for sham rTMS to a 1.4-point larger improvement in 2 studies.[42,44] However, findings were only statistically significant for 1 comparison in 1 study (10 Hz rTMS vs. sham rTMS, 1.4-point larger improvement favoring active treatment ($P < 0.001$). Authors of this same study observed a 0.4-point larger improvement for sham compared to 1 Hz rTMS treatment (P NR, but likely not significant).[42] Statistical significance testing was not reported for any comparisons in the second study.[43] The third study reporting VAS assessment of loudness reported percent change in score at an unreported follow-up timepoint; the findings ranged from a statistically significant larger 3.1% improvement for sham rTMS compared to 20 Hz rTMS to a statistically significant 6.7% and 7.3% larger improvements for 3 Hz and 1 Hz rTMS, respectively, compared to sham rTMS.[44] The differences between 5 Hz and 10 Hz rTMS participants and sham participants were not statistically significantly different. The fourth study reported using a VAS assessment of tinnitus discomfort.[41] This study reported significant improvement for active rTMS compared to sham immediately after treatment (1.3-point larger improvement, $P = 0.02$) and at week 1 (0.8-point larger improvement, $P = 0.02$). By the end of week 2, the sham group had a 3.3 larger

improvement compared to active rTMS, but this finding was not statistically significant (*P* = 0.60).

Three RCTs reported using the TQ at timepoints immediately after treatment through 3 months (months as the primary endpoint measure).[33,36,40] In the 2 studies that either reported the between-group difference in change in mean score or for which we could calculate it, the difference in change in scores ranged from a 0.6-point larger improvement for sham rTMS to an 3.4-point larger improvement for active rTMS. This difference was not statistically significant in 1 study (*P* = 0.10)[36] and statistical significant testing was not reported in the other study.[33] In the third study reporting using the TQ, the mean percentage difference in TQ score immediately after treatment was -19.4% (*P* = 0.022); however, all scores returned to baseline values within 2 weeks of treatment.[40]

One RCT reported using the TFI after the last treatment session and at 6 months followup.[29] Participants receiving active rTMS had a 3.4-point larger improvement in mean score compared to sham rTMS after the last treatment session (*P* = 0.23) and a 10.9-point larger improvement at 6 months (*P* = 0.007). The percentage of participants who experienced a 7-point or more improvement was higher among the active treatment group (56%) compared to the sham group (22%, *P* = 0.005) immediately after treatment and at 6 months (66% vs. 38%, respectively, *P* = 0.02).

Psychological Measures

Five RCTs[30,32,34,39,41] reported on depression using the Beck Depression Inventory (BDI)[30,32,34,39] or the Hamilton Depression Rating Scale (HAM-D).[41] Depression was not a primary study outcome in any of these studies. In all studies, no statistically significant differences between active rTMS and sham rTMS were observed.

One RCT reported an anxiety outcome using the Hamilton Anxiety Rating Scale (HAM-A) but it was not the primary study outcome.[41] At 2 weeks follow up, study authors observed no differences in scores between active rTMS and sham rTMS (between-group difference in scores 0 to -0.5 but no statistical significance testing was conducted).[41]

One RCT reported on sleep outcomes using the Jenkins Sleep Evaluation Questionnaire (JSEQ) but it was not the primary study outcome.[34] Study authors reported no statistically significant difference in sleep symptoms between active rTMS and sham rTMS (*P* = 0.63).[34]

Quality of Life

One parallel assignment RCT reported on QoL using the Short Form Survey-12 item (SF-12) physical health and mental health component scores.[32] Study authors reported no statistically significant differences in scores at 6 months between active rTMS and sham rTMS (*P* = 0.14), however, the magnitude of effect was not reported.

Safety Measures

Eight parallel assignment RCTs[26,28-34] and 6 crossover RCTs[36-41] reported on safety outcomes but these were not the primary study aim in any study and only some studies reported these

outcomes by group (i.e., active rTMS compared to sham rTMS). Further, studies did not consistently report whether the adverse events and side effects reported were ascertained only during the study treatment period (usually 1 session to 2 weeks) or were also ascertained in the weeks to months following completion of treatment.

Across studies, findings were mixed. Five studies reported that no side effects or adverse events related to treatment (active or sham groups).[29,36-38,40] Of those studies reporting adverse events, the most commonly reported events were headache, local irritation, tongue paresthesia, transient jaw soreness, jaw twitching, neck/shoulder tightness or twitching, and orbital twitching. Of the 6 studies reporting adverse events by group, 3 studies reported a similar proportion of adverse events. One of these studies reported similar incidence of adverse events (35.1% active vs. 39.5% sham) and serious adverse events (1.4% active vs. 1.3% sham)[32]; 1 study reported similar incidence of headache (12.5% active vs. 18.8% sham),[33] and 1 study reported no significant difference in adverse events (11 events active vs. 8 events sham, $P = 0.42$).[39] Two studies reported a higher incidence of side effects in the active rTMS group relative to sham (15.4% vs. 7.7%[26]; and 19.2% vs. 3.9%[31]). Finally, 1 study reported a higher incidence of side effects in the sham rTMS group (25%) compared to the active rTMS group (15%).[30] The remaining studies did not report adverse events by group. However, these studies reported findings such as "majority reported no side effects," "no sustained effects," "no major side effects."

3.4 Cognitive Behavioral Therapy Interventions

We identified 21 studies that described CBT interventions for the treatment of tinnitus, of which 19 were RCTs,[45-63] 1 was a cluster RCT,[64] and 1 was a controlled trial.[65] Nearly all studies used wait list control groups (i.e., delayed treatment), though some studies also included attention control groups. One of the RCTs evaluated tinnitus retraining therapy (TRT) in addition to a CBT intervention; the results for the TRT intervention arm are included in Section 3.5 of this report.[58] The key findings for CBT are:

- Thirteen RCTs[45,47,49,50,53,54,56-58,62,63,65,66] reported on group or individual, therapist-led CBT interventions. These interventions improved tinnitus-related distress and disability compared to control in a majority of studies, although findings were somewhat heterogenous across measures used.
- Nine RCTs[46,48-52,55,60,64] evaluated internet or book-guided self-directed interventions. These interventions also improved measures of tinnitus distress and disability compared to control, although findings were also heterogenous across measures and follow-up timepoints assessed.
- In 11 RCTs[45,49,50,53,54,56,57,59,61-63] that investigated therapist-led CBT interventions and that reported on psychological outcomes, most favored the intervention, although findings were only statistically significant in some studies.
- In 8 RCTs[46,48-51,55,60,64] that used internet or book-guided CBT and that reported on psychological outcomes, most favored the intervention, although findings were only statistically significant in some studies.

- In 2 RCTs[51,64] that used internet or book-guided CBT and that reported on QoL, no statistically significant findings between intervention and control were observed. No studies of therapist-led CBT reported QoL outcomes.
- In 3 RCTs[54,61,65] that used therapist-led interventions and that reported on adverse events, the frequency of adverse events was rare to none.
- No RCTs reported on cost outcomes.

The rest of this section provides detailed study characteristics and results.

3.4.1 Study and Population Characteristics

The CBT trials were conducted between 1996 and 2018. We assessed 8 studies[45,46,48-51,54,55] as having some risk of bias and 13 studies[47,52,53,56-65] as having high risk of bias. Four studies were conducted in the United States,[45,47,53,61] 7 in Germany,[48-50,54,58,59,65] 4 in Australia,[52,62-64] 4 in Sweden,[51,55,57,60] and 2 in the United Kingdom.[46,56] Industry funding was provided partially or fully in 3 studies[58,64,65] whereas non-industry funding was reported for 15 studies.[45-55,57,59-61] The source of funding was not reported for the remaining 3 studies.[56,62,63] ***Table 7*** includes the characteristics of included CBT studies, with additional details found in ***Appendix D, Tables D3a, D3b,*** and ***D3c.***

Across the studies, the sample sizes among eligible study arms ranged from 20 to 304. The mean or median age of participants ranged from 47 to 70 years. All studies included both female and male participants, (% female range: 5% to 60%). Of the 4 studies that reported data on race and ethnicity, the proportion of white participants ranged from 66% to 92%.[45,47,53,61] Eleven studies included participants with some degree of hearing loss,[45,47-50,57-60,62-65] 2 reported participants with a history of using hearing aids, and 1 reported both hearing loss and use of hearing aids.[55] One study included participants with tinnitus due to blast injury,[45] 2 studies excluded participants with such injuries,[46,65] and the rest of the studies did not report on this characteristic. The mean tinnitus duration ranged from 0.3 to 13 years; however, 5 studies did not report tinnitus duration.[45,52,61-63]

The CBT interventions included in this HTA comprise a variety of approaches such as relaxation techniques and coping strategies that patients may use to manage, rather than cure, their tinnitus. The CBT interventions were conducted over varying durations. Seven studies conducted CBT over 6 weeks or less[47,55,57,60-62,64] and 10 studies were conducted over 8 to 12 weeks.[46,48-54,58,63] One study utilized an active CBT intervention over 5 weeks but then provided a "booster" at months 3 and 6.[45] Finally, 3 studies did not report the intervention duration.[56,59,65] In 13 studies, CBT was delivered through various modalities that included in-person, therapist-led group sessions or workshops,[47,53,57-59,61-63] or individual CBT provided in person or by telephone.[45,54,56,65] Eight studies used self-directed CBT approaches, with minimal (phone or email) or no therapist-involvement; these included internet-based[46,48,51,60,64] and book-guided interventions.[52,55] One study included both an in-person group CBT arm and an internet-based CBT arm[49] and another study included 3 study arms: group-based CBT, internet-delivered CBT, and book-guided CBT.[50] Thirteen studies used delayed treatment controls,[45,47,50,52-54,56,57,60-63,65] 6 studies used 'attention' control groups that, for example, may have included only basic reading material or online discussion forums,[48,49,51,55,58,64] and 2 studies used controls who received no

treatment at all.[46,59] Authors of 8 studies reported fidelity to the intervention using a variety of measures including the number and duration of telephone calls, the proportion of self-help materials read, modules completed, or group meetings attended; with a few exceptions fidelity was moderate in most of these studies.[45,48,49,51-53,61,64]

Table 7. Summary of Study Characteristics of Included Studies of Cognitive Behavioral Therapy for the Treatment of Tinnitus

Author Year	Country	Risk of Bias	Eligible Interventions & Comparators (N randomized)	Total Sample Size[a]	Treatment Duration	Mean Age (SD)	N (%) Female	Outcomes Reported
Abbott et al. (2009)[64]	Australia	High	Information-only control (24) Internet-based CBT (32)	56	NR	Control: 48.7 (8.6) CBT: 50.5 (9.5)	5 (10*)	• Tinnitus distress • QoL • Psychological
Andersson et al. (2002)[60]	Sweden	High	Waitlist control (64) Group-based CBT (53)	117	NR	Control: 47.2 (15.0) CBT: 48.5 (12.3)	Control: 31*(48) CBT: 24*(46)	• Tinnitus distress • Psychological
Andersson et al. (2005)[57]	Sweden	High	Waitlist control (11) Internet-based CBT (12)	23	NR	70.1 (3.9)	11 (47.8*)	• Tinnitus distress • QoL • Psychological
Beukes et al. (2018)[46] Beukes (2018)[192]	U.K.	Some	Attention-only control (73) Internet-based CBT (73)	146	8 weeks	55.6 (12.9)	63 (43)	• Tinnitus distress • QoL • Psychological
Henry et al. (1996)[62]	Australia	High	Waitlist control (20) Group-based CBT (20)	60	NR	64.6 (NR)	8 (13*)	• Tinnitus distress • Psychological
Henry et al. (1998)[63]	Australia	High	Waitlist control (12) Group-based CBT (12)	24	NR	56.3 (NR)#	19 (38*)#	• Tinnitus distress • Psychological
Henry et al. (2017)[47]	U.S.	High	Waitlist control (150) Group-based CBT[b] (150)	300	8 weeks	58(13)#c	15* (5)	• Tinnitus distress
Henry et al. (2018)[45]	U.S.	Some	Waitlist control (104) Individual, telephone-based CBT[b] (101)	205	8 weeks	59.0 (10.5)	30 (14)	• Tinnitus distress • QoL • Psychological
Hesser et al. (2012)[51]	Sweden	Some	Online discussion forum control (32) Internet-based CBT (32)	64	8 weeks	48.5 (14.7)	43 (43.4)	• Tinnitus distress • QoL • Psychological
Jasper et al. (2014)[49] Conrad et al. (2015)[193]	Germany	Some	Online discussion forum control (44) Group-based CBT (43) Internet-based CBT (41)	128	10 weeks	Control: 52.1 (9.0) Group CBT: 50.2 (13.1) Internet CBT: 51.3 (9.8)	Control:16 (36.4) Group CBT:19 (44.2) Internet CBT:16 (39.0)	• Tinnitus distress • QoL • Psychological
Kaldo et al. (2007)[55]	Sweden	Some	Waitlist control (38) Book-guided CBT (34)	72	NR	Control: 48.5 (15.7) CBT: 45.9 (13)	Control: 18 (47) CBT: 17 (50)	• Tinnitus distress • QoL • Psychological

Author Year	Country	Risk of Bias	Eligible Interventions & Comparators (N randomized)	Total Sample Size[a]	Treatment Duration	Mean Age (SD)	N (%) Female	Outcomes Reported
Kroner-Herwig et al. (2003)[59]	Germany	High	Waitlist control (20) Group-based CBT (43)	116	NR	Control: 47.3 (7.9) CBT: 44.7 (12.7)	Control: 10*(50) CBT: 24*(55.8)	• Tinnitus distress • Psychological
Malouff et al. (2010)[52]	Australia	High	Waitlist control (78) Book-guided CBT (84)	162	8 weeks	Control: 57.8 (13.3) CBT: 57.3 (13.7)	72* (44*)	• Tinnitus distress • QoL
Martz et al. (2018)[61]	U.S.	High	Waitlist control (10) Group-based CBT (10)	20	NR	57.8 (16.4)#	8 (20)#	• QoL
Nyenhuis et al. (2013)[50]	Germany	Some	Information-only control (77) Book-guided CBT (77) Internet-based CBT (79) Group-based CBT (71)	304	Control, book, and internet CBT:12 weeks Group CBT: 4 weeks	48.5 (12.8)	132*(43*)	• Tinnitus distress • Psychological
Robinson et al. (2008)[53]	U.S.	High	Waitlist control (27) Group-based CBT (38)	65	8 weeks	55.0 (11.3)	31 (48)*	• Tinnitus distress • Psychological
Sadlier et al. (2008)[56]	U.K.	High	Waitlist control (11) Individual-based CBT (14)	25	NR	Control: 54.3 (15.3) CBT: 60 (14.6)	Control: 6 (55*) CBT: 11 (79*)	• Tinnitus distress • Psychological
Weise et al. (2008)[54]	Germany	Some	Waitlist control (67) Individual-based CBT (63)	130	3 months	Control: 52.9 (11.9) CBT: 49.5 (11.8)	Control: 26 (44.1) CBT: 23 (44.2)	• Tinnitus distress • Psychological
Weise et al. (2016)[48]	Germany	Some	Online discussion forum control (62) Internet-based CBT (62)	124	3 months	Control: 47.5 (14.1) CBT: 47.81 (12.3)	74* (60*)	• Tinnitus distress • QoL • Psychological
Zachriat et al. (2004)[58]	Germany	High	Education-only control (23) Group-based CBT (29) Tinnitus Retraining Therapy (31)	77	CBT: 12 weeks TRT: 6 months	Control: 56.1 (10.6) CBT: 53.8 (11.8) TRT: 51.6 (11.0)	Control: 5 (26)* CBT: 11 (41)* TRT: 10 (33)*	• Tinnitus distress
Zenner et al. (2013)[65]	Germany	High	Waitlist control (120) Individual-based CBT (166)	286	NR	Median 49 (Range 14 to 78)	98 (34)	• Tinnitus distress

Notes: * Indicates a data value that we calculated based on data provided in the publication. # Indicates that the data was only reported for study completers, not the number that was randomized. [a] From study arms eligible for inclusion in this HTA. [b] Provided as part of progressive tinnitus management clinical program. [c] The total number of participants was 297 but there was no baseline data on 3 participants that were randomized.

Abbreviations: SD = standard deviation; CBT = cognitive behavioral therapy; QoL: quality of life; TRT = tinnitus retraining therapy.

3.4.2 Findings

We identified 21 CBT studies overall and determined that their interventions could be organized into 2 primary modalities for delivering CBT interventions: therapist-led group or individual interventions (14 studies[45,47,49,50,53,54,56-59,61-63,65]) and self-directed interventions provided primarily by a website or book or both, with minimal to no therapist-involvement (9 studies[46,48-52,55,60,64]). Of note, 2 studies included both therapist-led and self-directed treatment arms and thus are included in the synthesis for both categories of intervention.[49,50] Across these categories, studies used a variety of tinnitus distress or disability measures, psychological measures, measures for quality of life, and safety. No studies reported cost measures. Detailed findings are reported in ***Appendix D, Tables D3d*** and ***D3e.***

3.4.2.1 Group or Individual Therapist-led Interventions

We identified 13 studies that provided group-based or individual therapist-led interventions, primarily in-person but 1 was provided predominantly by phone.[45,47,49,50,53,54,56-58,62,63,65,66] Three studies used an active control (discussion forum,[49] education only,[58] information only,[50]) and the rest used waitlist controls (i.e., delayed treatment). No studies in this category reported quality of life or cost outcomes.

Tinnitus Distress and Disability

Seven studies[50,53,54,56,58,59,65] reported results using the TQ; the TQ was designated as the primary study aim in 4 of those studies.[50,54,56,58] All but 1 study[53] reported statistically significant outcomes that favored the intervention. However, the time at which these outcomes were measured in relationship to completion of the intervention was not clear in 2 studies.[58,65] Three studies reported effect sizes ranging from 0.81 to 0.95.[50,54,58] As a reminder, a standardized effect size of 1.0 indicates that the 2 groups differ by 1 standard deviation and an effect size greater than 0.80 is considered a large effect.[149,150] One of these studies[54] also reported a statistically significant effect size for a VAS assessment of distress (effect size 0.45 [small effect], $P < 0.01$) whereas the others did not report additional measures of tinnitus distress or disability. A fourth study reported a 9.2 point larger improvement in change in TQ score for the treatment group compared to control ($P < 0.01$) and statistically significant differences on a VAS assessment for tinnitus control, but no significant differences on the Tinnitus Disability Questionnaire (TDQ) or VAS assessments for loudness or awareness.[59] The fifth study reported the median quartile change in TQ score (OR 2.0, 95% CI, 1.6 to 2.5); this study found similar findings on the other measures of tinnitus reported (loudness, annoyance, change).[65] The sixth study did not report any additional measures of tinnitus distress or disability.[56] In the seventh study (and the smallest n = 65), no significant differences were reported for the TQ or for most of the other tinnitus measures used (THQ, TQ, VAS assessment for severity and annoyance) but a significant difference was reported for the TRQ.[53]

Three studies reported results using the THI,[45,47,49,53] but it was only designated as the primary study outcome in 1 of those studies.[49] A statistically significant difference in change in mean THI score was observed in 2 of the 3 studies, although only 2 provided values for effect sizes (0.38 [small effect], 95% CI, 0.12 to 0.64[47] and 0.98 [large effect], 95% CI, 0.66 to 1.29[45]) at 6 months. In 1 of these studies, a significantly higher proportion of participants in the treatment group (44%) achieved a clinically meaningful reduction in THI score compared to the control

group; (8%, *P*<0.001) similar findings were reported for the TFI.[45] In this study, the intervention consisted of telephone appointments in which either an audiologist or psychologist provided skills education for self-management over 5 weeks. The audiologists or psychologists could additionally provide "in-depth evaluations" and "individualized support."[45] In the other study providing an effect size, a higher proportion of participants in treatment also achieved a clinically meaningful decrease (17.1%) compared to the control participants (9.1%), but this finding was not statistically significant.[47] However, this study's primary outcome was the TFI and those findings indicated a statistically significant improvement for intervention participants whether measured by change in mean score or by proportion achieving a clinically meaningful reduction.[47] The other 2 studies that used THI also reported using other measures of tinnitus distress or disability. In 1 study, a significant difference in change in score was observed for the THI (effect size 0.69 [medium effect], 95% CI, 0.25 to 1.12, $P < 0.001$) and for the mini-TQ (effect size 0.93 [large effect], 95% CI, 0.49 to 1.37) but not for the Tinnitus Acceptance Questionnaire (TAQ).[49]

Four studies reported findings based on the TRQ[53,57,62,63]; 1 was described previously and reported statistically significant difference for the TRQ but not for any of the other tinnitus-related measures reported.[53] Of the other 3 studies, the between-group differences in change in mean score ranged from a 7.8- to 10.3-larger point improvement for intervention groups compared to control groups; this finding was statistically significant in 1 study.[57] Significance testing was not reported by the other 2 studies and the studies did not provide the data needed for us to conduct the testing. In these 2 studies, which were conducted by the same author and consisted of 6 to 8 weeks of structured group CBT sessions, participants in the intervention groups had larger improvements on the THQ, Tinnitus Effects Questionnaire (TEfQ), TCQ, and the Tinnitus Coping Style Questionnaire (TCSQ); again, no statistical significance testing was conducted by the authors.[62,63]

Psychological Outcomes

Psychological outcomes were reported by 11 studies but were not the primary study aim in any study.[45,49,50,53,54,56,57,59,61-63] Ten studies reported outcomes related to depression using the HADS-D, BDI, ADS, HAM-D, or PHQ-D measures.[45,49,50,53,54,56,57,59,62,63] Although the direction and magnitude of effect was similar across nearly all studies (larger improvements for treatment groups compared to control groups), these differences were only statistically significant in 4 studies.[45,50,53,54]

Four studies reported outcomes related to anxiety using the HADS-A and the ASI. These studies also reported larger improvements for treatment groups compared to controls, but the findings were statistically significant in only 2 studies.[45,49] One of the 4 studies reported both the HADS-A and the ASI; significant findings favoring the intervention group were observed for the latter measure but not the former measure.[57]

Three studies reported on general well-being using the SCL-90R measure.[53,54,59] Two studies[53,54] reported a significant difference between treatment and control groups favoring the intervention whereas 1 reported a nonsignificant difference in improvement.[59]

Three studies reported on impact of treatment on measures related to sleep (Epworth Sleepiness Scale, Insomnia Severity Index, Sleep Quality).[45,49,57] One study[49] reported statistically significant larger improvements with treatment (effect size 0.60 [medium effect], *P* = 0.001) compared to control whereas the other 2 studies reported no significant differences between-groups.

Two studies reported on coping levels using the COPE measure.[59,61] One study[59] reported significant improvements immediately post-treatment for the treatment group compared to control (effect size 1.04 [large effect]) whereas the other study reported no significant differences either at the end of treatment or at 4 weeks post-treatment.[61]

Quality of Life

No studies in this group of therapist-led interventions reported quality of life outcomes.

Safety

Only 3 studies reported on any adverse events, which were minimal.[54,61,65] One study reported 40 adverse events overall (not by group) of which the authors considered 1 ("unpleasant images") as treatment-related.[65] The remaining nontreatment-related adverse events in this study included upper respiratory infections, allergies, eczema, accidents, depression, and sudden hearing loss. In the second study, the authors used an adverse effects scale (range from 1 [no effects] to 6 [large effects]) and determined most patients did not experience negative treatment side effects (mean = 1.5, SD = 0.6).[54] Lastly, in the third study, 0 adverse events were reported.[61]

3.4.2.2 Self-Directed CBT Interventions

Nine studies primarily used self-directed CBT interventions delivered primarily through self-guided activities provided over the internet or through a book provided to participants.[46,48-52,55,60,64] Some of these interventions also included limited therapist contact (periodic emails or telephone followup). Three studies in this category used a waitlist control (i.e., delayed treatment)[52,55,60] whereas the other studies used active control groups (i.e., online discussion forums, information only, periodic monitoring). No studies in this category reported safety or cost outcomes.

Tinnitus Distress and Disability

Four studies reported findings using the THI[48,49,51,55]; this measure was the primary study aim for 2 of the studies. All 4 studies reported statistically significant larger improvements for treatment groups compared to control groups (effect size range 0.56 to 0.70 [medium effect]). One study reported that 44% of the treatment group achieved a clinically meaningful reduction compared to 16% of the control group (*P* = 0.014).[51] Three of these 4 studies also reported statistically significant larger improvements on other measures of tinnitus-related distress and disability (mini-TQ,[48,49] TAQ,[48,49] TRQ,[55] VAS for loudness,[55] and VAS for distress.[55]

Four studies reported findings using the TRQ.[52,55,60,64] One study found a statistically significant difference favoring the intervention with a mean difference of 11.6 points (95% CI, -18.49 to -4.71, *P* = 0.001). Further,11 of 34 (32%) in the treatment group reported a clinically meaningful change compared to 2 of 38 (5%) in the control group; the difference was statistically significant

(P = 0.003).[55] Another study reported a statistically significant larger improvement (12.5 points) among the treatment group compared to the control group (P=0.002); however, the proportion of participants achieving a clinically meaningful reduction was not statistically different between groups (13% vs. 3%, P = 0.29).[60]

One study each reported the TFI[46] and TQ[50]; both measures were primary study aims in these studies and neither study reported any other additional measures of tinnitus distress or disability. The effect size in the study reporting the TFI was 0.7 [medium effect], but this effect was not statistically significant (P = 0.05). In the study reporting the TQ, a statistically significant larger improvement was observed at both 3 months and 9 months for internet-based treatment compared to control (effect sizes 1.04 [large effect] and 0.66 [medium effect], respectively); the effect size at 3 months for the book-guided treatment was 0.24 at 3 months and 0.39 at 9 months, but only the latter was statistically significant.[50] Both the internet- and book-guided treatments resulted in a statistically significant higher proportion of participants achieving a clinically meaningful improvement in score at both 3 and 9 months followup compared to the control group.

Psychological Outcomes

Psychological outcomes were reported by 8 studies in this category but were not the primary aim in any study.[46,48-51,55,60,64] Seven studies reported outcomes related to depression using the HADS-D, PHQ-D, and PHQ-9 measures.[46,48-51,55,60] Although the direction and magnitude of effect was similar across nearly all studies (larger improvements for treatment groups compared to control groups), these differences were only statistically significant in 3 studies.[50,55,60]

Five studies[46,48,49,51,60] reported outcomes related to anxiety using the HADS-A, GAD-7, and the ASI. Two studies reported significantly larger improvements for treatment groups compared to control groups[51,60]; the other 3 studies also reported numerically larger improvements, but these findings were not statistically significantly.

Four studies reported the impact of treatment on sleep with the ISI[46,48,49,51] and 2 studies reported with a VAS for sleep quality.[60,64] Three of the 4 studies using the ISI reported significantly larger improvements (effect sizes ~ 0.60 [medium effect]) for treatment compared to control groups.[46,48,49] The effect size in the fourth study was 0.4 [small effect], but was not statistically significant.[51] The 2 studies reporting using a VAS assessment for sleep quality reported no significant differences between groups.[60,64]

Three studies reported using other psychological measures including the perceived stress scale (PSS),[51] the Depression, Anxiety and Stress Scale (DASS)[64] and a VAS assessment for stress.[55] Findings between treatment and control groups in all studies were not statistically different.

Quality of Life

Two studies reported on quality of life.[51,64] In the first study, authors reported a larger improvement on the Quality of Life Inventory for the treatment group (effect size 0.45 [small effect]), but this finding was not statistically significant (P = 0.08). In the second study, authors

reported no statistically significant differences between treatment and control groups on the World Health Organization Quality of life (WHO QoL) measure (P = 0.68).[64]

3.5 Tinnitus-Specific Interventions

We identified 10 RCTs (reported in 11 publications) describing results from studies that focused on tinnitus-specific therapies.[24,58,67-74] The interventions evaluated included tinnitus retraining therapy (8 studies[58,67-73]), neuromonics treatment (1 study[24]), and a tinnitus retraining music-based therapy (1 study[74]). One study that evaluated TRT also included an additional tinnitus-specific intervention called tinnitus masking.[67] In addition to the tinnitus-specific interventions evaluated, 1 study also included an eligible sound therapy study arm,[24] and 1 study included an eligible CBT intervention study arm.[58] Results for those 2 study arms are reported in the sound therapy (Section 3.2) and CBT (Section 3.4) sections of this report, respectively. Key findings are:

- All studies reported measures of tinnitus distress or disability as the primary outcome. Eight studies found statistically significant favorable effects of the intervention on at least 1 measure; however, the significance and magnitude of the effect varied by measure, timepoint, and comparison group. One study did not conduct significance testing but found a larger improvement in the intervention group and the remaining study found no statistically significant difference in effect, on this or any other type of tinnitus-specific measure.
- Three RCTs[68-70] reported on psychological measures. Two studies found statistically significant favorable effects for the intervention on some measures or time points but not all, and the third study found no difference in effect between intervention and control group, which was consistent with other measures reported from this study.
- Two RCTs[68,69] reported on quality of life measures. One study found no difference in effect between intervention and control group, which was consistent with all other measures reported from this study. The second study found larger statistically significant improvements in the intervention group at 8 and 12 months for the intervention group compared to the control group.
- One RCT[68] that compared tinnitus retraining therapy to usual care over 8 months duration reported safety and cost outcomes. This study reported that no adverse events occurred, and the cost per quality-adjusted life year (QALY) gained from health care payor perspective was $10,456 (95% CI, NR), with 58% to 68% probability of being cost-effective using a $45,000 willingness to pay threshold.

The rest of this section provides detailed study and population characteristics and results.

3.5.1 Study and Population Characteristics

The included tinnitus-specific therapy trials were conducted between 2004 and 2017. All were parallel-assignment RCTs and we assessed 0 of these trials as low risk of bias, 4 as having some risk of bias,[67-69,73] and 6 as having high risk of bias.[24,58,70-72,74] Three trials were conducted in the U.S.,[67,71,73] 4 in Germany,[58,70,72,74] 1 in the Netherlands,[68] 1 in Australia,[24] and 1 in Sweden.[69] Five studies received no industry funding,[67,68,71,73,74] 2 studies were partially funded by industry,[58,69] 1 study was entirely funded by industry,[24] and 2 studies did not report source of

funding.[70,72] ***Table 8*** summarizes the characteristics of included tinnitus-specific therapy RCTs, with additional details found in ***Appendix D, Tables D4a, D4b,*** and ***D4c.***

Table 8. Summary of Study Characteristics of Included Studies of Tinnitus-specific Interventions for the Treatment of Tinnitus

Author Year	Country	Risk of Bias	Eligible Interventions & Comparators (N randomized)	Total Sample Size[a]	Treatment Duration	Mean Age (SD)	N (%) Female	Outcomes Reported
Bauer et al. (2017)[73]	U.S.	Some	Standard care (19) Tinnitus retraining therapy (20)	39	18 months	N (%) in age categories 18 to 50 years: 6 (16)* 51 to 65 years: 25 (66)* 66 to 75 years: 7 (18)*	12 (32)*	Tinnitus distress
Caffier et al. (2006)[72]	Germany	High	Waitlist control (20[b]) Tinnitus retraining therapy (20[b])	48	12 months	51 (NR)	22 (46*)	Tinnitus distress
Cima et al. (2012)[68] Maes (2014)[194]	The Nether-lands	Some	Usual care (247) Tinnitus retraining therapy + CBT (245)	492	8 months	54.2 (11.5)	184 (37)*	• Tinnitus distress • Psychological • Safety • Cost
Davis et al. (2008)[24]	Australia	High	Counseling only (13) Neuromonics (22)	69	12 months	49.8 (15.8)	24 (48.0*)	Tinnitus distress
Henry et al. (2016)[67]	U.S.	Some	Waitlist control (33) Tinnitus education (39) Tinnitus retraining therapy (34) Tinnitus masking (42)	148	18 months	61.7 (9.8)	4 (2.7)*	Tinnitus distress
Henry et al. (2007)[71]	U.S.	High	No treatment (91) Traditional support (84) Tinnitus retraining therapy (94)	269	4 weeks	61.6 (9.9)	9 (3)	Tinnitus distress
Krick et al. (2015)[74]	Germany	High	Waitlist control (25) Tinnitus retraining- based music therapy (25)	50	1 week	Control: 42.6 (11.5) Music therapy: 43.9 (10.4)	Control: 9(41*) Music therapy: 9(45*)	Tinnitus distress
Seydel et al. (2010)[70]	Germany	High	Waitlist control (45) Tinnitus retraining therapy (45)	90	7 days	51 (NR)	119 (50*)	• Tinnitus distress • Psychological
Westin (2011)[69]	Sweden	Some	Waitlist control (22) Tinnitus retraining therapy (20)	64	18 months	Control: 49.6 (11.9) Tinnitus retraining therapy: 49.0 (14.5)	Control: 8 (36) Tinnitus retraining therapy: 8 (40)	• Tinnitus distress • Psychological • QoL
Zachriat (2004)[58]	Germany	High	Education-only (23) Tinnitus retraining therapy (31)	77	24 weeks	Control: 56.1 (10.6) Tinnitus retraining therapy: 51.6 (11.0)	Control: 5 (26)* Tinnitus retraining therapy: 10 (33)*	Tinnitus distress

Notes: * Indicates a data value that we calculated based on data provided in the publication. [a] From study arms eligible for inclusion in this HTA. [b] After post-randomization exclusions.

Abbreviations: CBT = cognitive behavioral therapy; NR = not reported; U.S. = United States.

Of the included studies, the sample sizes ranged from 39 to 492 participants. Seven studies had sample sizes of less than 100 participants.[24,58,69,70,72-74] The mean age of included populations ranged from 43 years to 62 years. All studies were conducted among both men and women; however, 2 studies, which were conducted primarily among U.S. military veterans, each had samples that were only 3% female.[67,71] Two studies reported data about participant race; 1 study was 100% white[73] and the other was 87% white.[67] One study had hearing loss as an explicit inclusion criterion[73] and 9 studies included patients with some degree of hearing loss, although hearing loss was not an explicit inclusion criterion.[24,58,67-72,74] Four studies excluded patients with profound hearing loss that precluded participation in the intervention (i.e., participating in group sessions or use of a sound generator device)[24,58,69,74] and 1 study included patients with profound hearing loss only if they were properly fitted with hearing aids.[70] One study included patients with blast injury[74] whereas the remaining studies did not report blast injury as part of their study characteristics.

Intervention durations ranged from 7 days to 18 months across this body of evidence. Study authors reported moderate adherence to interventions in 2 studies[24,69]; adherence was not reported in the remaining studies.

Seven studies used tinnitus-specific interventions that included the use of sound maskers or generators.[24,58,67-69,72,73] The sound device in 1 study included an acoustic stimulation device in the form of music in an intervention termed "neuromonics."[24] Four studies used a combination device that was a sound generator or masker for normal hearing patients and a sound generator or masker and hearing aid for those with hearing loss.[67,68,72,73] The final 2 studies included sound generators for all participants regardless of hearing loss, although both excluded participants with profound hearing loss that would preclude sound generator use or group communication.[58,69] All studies included education and counseling about use of the sound device. In addition to the sound device, these interventions all included an education and counseling component, many based on CBT principles, focused on coping skills and auditory training for managing the distress related to tinnitus. One study[67] included an intervention arm in which 1 group received structured counseling to teach TRT specific concepts and the second group received structured counseling of the same format and length to teach tinnitus-masking specific concepts such as how to use sound therapy to relieve tinnitus symptoms.

Of the remaining 3 studies that did not use sound maskers or generators, 1 included TRT that provided detailed information about sound generators to participants but it was unclear if sound generators were provided,[71] and 2 studies used tinnitus-specific interventions without sound generators.[70,74]

3.5.2 Findings

We identified 10 RCTs overall and determined that their interventions could be organized into 2 categories: tinnitus-specific interventions with sound generators or maskers (7 studies[24,58,67-69,72,73]) and tinnitus-specific interventions without sound generators or maskers (3 studies[70,71,74]). Across these 2 categories, studies used a variety of tinnitus distress or disability measures, psychological measures, and measures for quality of life. One study included measures of safety and cost.[68] Detailed results are provided in ***Appendix D, Tables D4d*** and ***D4e***.

3.5.2.1 Tinnitus-specific Interventions With Sound Generators or Maskers

We identified 7 studies that provided tinnitus-specific interventions that included psychological counseling with sound generators or maskers. Among these, 3 studies used waitlist control groups (i.e., delayed treatment),[67,69,72] 2 studies used attention or active control groups consisting of education or counseling only,[24,58] 1 study compared TRT to standard care with a sham sound generator device,[73] and 1 compared TRT with sound generators to a usual care control group that received sound generators plus some counseling and individual consultations as needed.[68]

Tinnitus Distress and Disability

Four studies reported using the THI and this was designated as the primary study aim in all 4 studies.[67-69,73] Three of the 4 studies found statistically significant favorable effects of the intervention at most, but not all timepoints.[67,68,73] The study that compared TRT to usual care (which included some counseling and sound generators) reported a statistically significant effect size ranging from 0.32 to 0.52 [small to medium effects] at 3, 8, and 12 months on the THI; the intervention duration was 8 months in this study and similar findings were observed on the TQ, TCS, and Tinnitus-related Fear Index (TRFI).[68] The 2 studies comparing TRT to a waitlist control both provided interventions over 18 months, but reported mixed findings. One study reported statistically significant larger improvements for both a TRT and tinnitus-masking counseling intervention at 3 months (effect size 0.52 [medium effect] and 0.44 [small effect], respectively) and 6 months (effect size 0.56 and 0.52 [medium effects], respectively).[67] This study also compared the TRT and tinnitus-masking counseling to an attention control and observed that effects were attenuated and no longer statistically significant (effect sizes 0.24 and 0.16 at 3 months, 0.16 and 0.11 at 6 months, and 0.22 and 0.11 at 18 months, respectively, all small to very small effects).[67] The other study also reported larger improvements in THI scores for the intervention compared to control (6.8 points at 6 months, 9.5 points at 12 months, 13.5 points at 18 months), but these findings were only statistically significant at 12 and 18 months.[73] The control group in this study was an active control for which participants received 3 aural rehabilitation sessions and a sham sound device. This study reported similar findings on the TFI.[73] Study authors also reported using the Tinnitus Experience Questionnaire (TEQ) and Tinnitus Interview Questionnaire (TIQ) in this study; larger improvements were observed across all timepoints for the intervention group compared to the control group; but only some of these differences were statistically significant.[73] The fourth study in this category (provided over 10 weeks' duration using a waitlist control group) reported a 5.1-point larger improvement for the TRT intervention group compared to control; but this finding was not statistically significant ($P = 0.44$) and was only 2.8 points larger when we adjusted for baseline difference in scores.[69] This study also reported using the TAQ and reported a 0.3-point improvement, but this finding was also not statistically significant ($P = 0.93$).[69]

Two studies reported using the TQ as their primary study aim and neither reported any additional measures of tinnitus distress or disability.[58,72] Both reported a statistically significant favorable impact of the intervention. One study compared counseling sessions every 3 months for 12 months, plus use of noise generators or combination devices depending on participant's hearing loss, to a waitlist control group; authors reported a significant ($P < 0.001$) favorable effect of the intervention but did not report the magnitude of the effect.[72] The second study compared 5 group counseling sessions over a 4- to 6-week period, plus sound generators, to an active control group

that received 1 general education session. This study found a larger improvement (8.1 points, *P* = 0.015) for the intervention group compared to the control group at 15 weeks, after participants had completed 4 of 5 TRT sessions.[58]

One study reported using the TRQ and 3 VAS assessments (tinnitus loudness, tinnitus severity, and general relaxation level).[24] This study compared an intervention termed 'neuromonics', which included tinnitus-specific counseling based on CBT principles and acoustic stimulus devices in the form of music, to an active control, which only included counseling. The neuromonics group had a lower mean score on the TRQ at 6 months followup according to a figure presented by the authors, but the numeric differences in scores and statistical significance testing were not reported. The authors also reported that 64% of the intervention group had a clinically meaningful reduction in score at 6 months, compared to 33% in the active control group, but this finding was not statistically significant (*P* = 0.07).[24] At 12 months, the authors reported a statistically significant lower mean score on the TRQ for the intervention compared to the control group (*P* = 0.014), but the magnitude of the difference was not reported.[24] Repeated measures on the VAS assessments over 12 months showed a significant favorable effect for the intervention on tinnitus loudness (*P* <0.001), tinnitus severity (*P* <0.001), and general relaxation levels (*P* = 0.003).[24]

Psychological Outcomes

Two studies reported using psychological measures.[68,69] Both reported on depression outcomes using the HADS-D. The study comparing TRT to usual care, conducted over 8 months, reported statistically larger improvements at 8 and 12 months (effect sizes 0.35 [small effect], *P* = 0.0002; and 0.24 [small effect], *P* = 0.0043, respectively) but not at 3 months (effect size 0.15 [very small], *P* = 0.09).[68] In the other study comparing TRT to waitlist control, conducted over 10 weeks, the authors observed no significant differences in HADS-D scores at 10 weeks followup (*P* = 0.77). In this study, authors also observed no effect on anxiety (HADS-A, *P* = 0.90) or sleep (ISI, *P* = 0 .49).[69]

Quality of Life

Two studies reported using quality of life measures.[68,69] The 10-week study that compared TRT to a waitlist control reported using the Quality of Life Inventory (QoLI) and observed no significant differences in this measure at 10 weeks followup (*P* = .31).[69] The 8-month study that compared TRT to usual care reported larger improvements as measured by the HUI at 8 months (0.04, *P* = 0.0258) and 12 months (0.06, *P* = 0.0009) but not at 3 months (0.01 smaller improvement, *P* = 0.6420).[68]

Safety

Only 1 study reported harms. The study, which compared TRT to usual care over an 8-month duration, reported that no adverse events occurred as a result of the intervention.[68]

Cost

One study reported cost outcomes.[68] This study comparing TRT to usual care over 8 months duration reported that the mean total health care costs per patient in 2009 USD over the duration of the intervention was $3,875 for usual care and $4,023 for TRT, resulting in a difference of

$152 (95% CI, $-333 to $643). The cost per quality-adjusted life year (QALY) gained from health care payor perspective was $10,456 (95% CI, NR) for the TRT intervention compared to usual care. Given a willingness-to-pay threshold of $45,000, there was a 68% probability that TRT is cost-effective. With regard to societal costs, the cost per patient over the duration of the intervention was $7,027 for usual care and $7,380 for TRT, resulting in a difference of $357 (95% CI, -$1,034 to $1,782). The cost per QALY gained from societal perspective was $24,580 (95% CI, NR) for the TRT intervention compared to usual care. Given a willingness-to-pay threshold of $45,000, there was a 58% probability that TRT is cost-effective.[68]

3.5.2.2 Tinnitus-specific Interventions Without Sound Devices

Three studies compared tinnitus-specific interventions without sound devices. One study compared TRT to both an attention control and to a no-treatment control,[71] 1 study compared TRT to a waitlist control (i.e., delayed treatment),[70] and 1 study compared the Heidelberg music therapy intervention to a waitlist control.[74] The TRT interventions were similar to those described in the previous section. The music therapy intervention consisted of techniques for processing sound, vocal exercises, training on intonation and listening capacity, musically based relaxation, and individualized tinnitus counseling.[74] Compared to the studies that used sound devices, this category of interventions was delivered over a shorter duration of 1 to 4 weeks, although 1 study included booster counseling sessions at 3, 6, and 12 months.[70] Studies in this category only reported tinnitus distress and disability measures, and psychological measures. No quality of life, safety, or cost outcomes were reported.

Tinnitus Distress and Disability

Two studies reported using the TQ.[70,74] The music therapy intervention reported a 16-point larger improvement on the TQ compared to a waitlist control immediately after the 1-week intervention; however, no statistical significance testing was reported and we were not able to calculate it based on data provided in the study. The second study reported a statistically significant effect ($P < 0.01$) favoring the TRT intervention compared to a waitlist control at 3 months, but did not report the magnitude of the effect.[70] Neither of these 2 studies reported any additional measures of tinnitus distress or disability.

The third study in this category, which compared a 4-week TRT intervention to both a no treatment control group and an attention control group, reported using the Tinnitus Severity Index (TSI).[71] We note that in this study it was unclear if the intervention group received only education about sound maskers or also received sound masker devices. Compared to the attention control group, the intervention group had a 0.6-point larger improvement ($P = 0.47$) at 6 months and a 0.3-point larger improvement at 12 months ($P = 0.033$). Compared to the no-treatment control group, the intervention group had a 3.3-point larger improvement at 6 months ($P = 0.001$) and a 2.4-point larger improvement at 12 months ($P = 0.013$).

Psychological Outcomes

One study that compared TRT to a waitlist control reported psychological measures.[70] Data for both the ADS (depression) and the PSS (stress) were only reported in graphs. A statistically significant effect was reported for the ADS ($P < 0.05$) but not for the PSS.[70]

4. Discussion

4.1 Summary of the Evidence

The certainty of evidence (i.e., GRADE rating) for the effectiveness of the interventions included in this HTA ranged from very low to low. A summary of the certainty ratings is provided in ***Table 9***; detailed GRADE ratings are provided in ***Appendix H.***

Table 9. Summary of GRADE Certainty Ratings for Non-invasive, Non-pharmacologic Interventions for Tinnitus Included in This HTA

Intervention (Comparison)	Outcome	No. Studies (No. Participants)	Certainty of Evidence[a]	Direction
Sound therapy interventions				
Hearing aids with sound-generating features (regular hearing aids)	Tinnitus distress and disability	3 RCTs (87)	●○○○	No benefit
Altered auditory stimulus (control stimulus)	Tinnitus distress and disability	4 RCTs (219)	●○○○	Unable to determine
	Psychological measures	1 RCT (50)	●○○○	No benefit
	Safety	1 RCT (100)	●○○○	No harms
Sound generators with information, education, counseling (information, education, counseling alone)	Tinnitus distress and disability	3 RCTs (234)	●○○○	No benefit
	Psychological measures	1 RCT (48)	●○○○	Unable to determine
Auditory Attention Training Game (control game)	Tinnitus distress and disability	1 RCT (31)	●○○○	Unable to determine
Repetitive transcranial magnetic stimulation interventions				
Active rTMS (sham rTMS)	Tinnitus distress and disability	18 RCTs (760)	●●○○	No benefit
	Psychological measures	5 RCTs (247)	●○○○	No benefit
	Quality of life	1 RCT (153)	●○○○	No benefit
	Safety	14 RCTs (526)	●○○○	Unable to determine
Cognitive behavioral therapy interventions				
Therapist-led individual or group CBT interventions (delayed treatment or attention control)	Tinnitus distress and disability	13 RCTs (1,743)	●●○○	Benefit
	Psychological measures	11 RCTs (1,100)	●●○○	Benefit
	Safety	3 RCTs (436)	●●○○	No harms
Internet or book-guided CBT interventions (delayed treatment or attention control)	Tinnitus distress and disability	9 RCTs (946)	●●○○	Benefit
	Psychological measures	8 RCTs (784)	●●○○	Benefit
	Quality of life	2 RCTs (120)	●○○○	No benefit
Tinnitus-specific interventions (tinnitus retraining therapy and others)				
Tinnitus-specific-interventions with sound therapy (delayed treatment or attention control)	Tinnitus distress and disability	7 RCTs (937)	●●○○	Benefit
	Psychological measures	2 RCTs (556)	●○○○	Unable to determine
	Quality of life	2 RCTs (556)	●○○○	Unable to determine
	Safety	1 RCT (492)	●○○○	Unable to determine
	Cost	1 RCT (492)	●○○○	Unable to determine

Intervention (Comparison)	Outcome	No. Studies (No. Participants)	Certainty of Evidence[a]	Direction
Tinnitus-specific interventions without sound therapy (delayed treatment or attention control)	Tinnitus distress and disability	3 RCTs (409)	●○○○	Benefit
	Psychological measures	1 RCT (90)	●○○○	Unable to determine

Notes: [a]Certainty ratings: ●○○○ Very low, ●●○○ Low, ●●○○ Moderate. ●●●● High

Abbreviations: CBT = cognitive behavioral therapy; RCT = randomized controlled trial; rTMS = repetitive transcranial magnetic stimulation.

The largest body of evidence was for CBT interventions; however, despite the number of available studies, small sample sizes and methodological study limitations limited our ability to have anything more than low certainty that CBT interventions provide a benefit for reducing tinnitus-related distress and disability and for improving psychological and emotional well-being with no harms. We also rated the certainty of tinnitus-specific interventions with or without sound therapy as *low* for benefit on tinnitus-related distress and disability, but we were unable to determine the impact of such interventions on other outcome domains due to inconsistency, imprecision, and methodological study limitations. However, given that these interventions include a large counseling component that is often based on CBT principles, it may be that any effectiveness of such interventions stems from the counseling component as opposed to the sound therapy components. We rated the evidence for sound therapy and rTMS interventions as *very low* for no benefit on efficacy outcomes. For rTMS we rated the evidence as *very low* for safety outcomes, but findings were mixed precluding a definitive conclusion regarding harms.

Our findings are largely consistent with findings from other systematic reviews on the treatment of tinnitus, some of which are summarized here. The authors of a 2018 Cochrane review on sound therapies (8 trials),[195] a 2014 Cochrane review of hearing aids (1 trials),[77] and a 2013 Agency for Healthcare Research and Quality (AHRQ) comparative effectiveness review (4 trials of sound therapies)[76] found no benefit of sound therapy in the treatment of tinnitus. A 2011 Cochrane review of rTMS (5 trials)[78] and the 2013 AHRQ review (6 trials of rTMS)[76] concluded limited support for rTMS in the treatment of tinnitus. More recently, a 2019 review by Schoisswohl et al. focused on characterizing the parameters used for rTMS in tinnitus trials.[196] This review, which was broader in scope than our HTA, was not limited to controlled trials and included 57 articles reporting on 74 study arms (e.g., some studies included multiple study arms evaluating different frequencies of stimulation). This review concluded that active rTMS was probably more effective than sham rTMS on the basis of the number of significant pre-post contrasts (within-group difference) in the active intervention arms compared to the number of significant pre-post contrasts in sham study arms. Note, single arm studies did not have sham study arms and this review did not consider the magnitude of between-group differences comparing active stimulation to sham stimulation. Two recent reviews, 1 of which supported the development of European guidelines on the use of rTMS, included literature published through 2016 and identified 26 placebo-controlled trials with at least 10 persons receiving active rTMS stimulation.[79,80] The authors of these reviews concluded that rTMS has possible therapeutic efficacy, but effects were partial and transient, with numerous uncertainties about its feasibility and usefulness in clinical practice.[79] In a 2010 Cochrane review (8 trials) of CBT for tinnitus, there was no evidence of a significant improvement in subjective loudness of tinnitus, but there

were improvements in depression and quality of life.[81] In the 2013 AHRQ review (10 studies of CBT) the authors reported low strength of evidence that CBT improved tinnitus-specific measures compared to controls and low strength of evidence for effect on depression, sleep, and global quality of life.[76] A 2010 Cochrane review of TRT only included 1 trial and concluded that TRT was more effective than sound masking alone.[82] The 2013 AHRQ review included 5 trials for TRT and found the evidence 'insufficient' for making a determination about the effectiveness of TRT.

4.2 Limitations of the Evidence Base

This HTA included many RCTs with high risk of bias and studies with small sample sizes resulting in imprecise effect estimates. The sources of bias varied across studies, but lack of robust randomization and allocation concealment processes or description of baseline characteristics reported by group to assess adequacy of randomization was a common issue. Studies using delayed treatment controls could not be blinded, and because patient-reported outcomes were used, outcome assessment could also not be blinded. Though most rTMS trials were blinded, many were crossover trials and the process of motor threshold titration to determine stimulation intensity compromises the blinding in such studies. Few trials were conducted according to a prespecified protocol and analysis plan, increasing the risk for reporting bias. Lastly, some studies had high attrition rates or did not report sufficient information to be able to assess attrition.

Another limitation of the evidence base is the heterogeneity of interventions evaluated. This was true for all 4 intervention categories we included. The heterogeneity in interventions may reflect the challenge involved in treating a heterogeneous condition, and the evolving search for effective treatments. For example, even within the rTMS category, there were differences in the stimulation parameters, the number of sessions received, and the timing of follow-up treatment. Authors of behavioral interventions demonstrating some effectiveness should manualize their approach and conduct larger replication studies that include robust measures of fidelity. In contrast, technology-based interventions may need additional basic science and clinical research to better understand the condition of tinnitus in order to develop targeted and effective technology-based treatments.

Lastly, the evidence provided no information about the effectiveness of treatments in subpopulations of particular interest, including those with occupational exposure to noise.

4.3 Clinical Practice Guidelines and Related Health Technology Assessments

We identified 5 clinical practice guidelines (CPGs) related to tinnitus diagnosis and treatment that evaluated the interventions included within the scope of this HTA. These are summarized in ***Table 10***.[79] We rated the quality of each guideline using the Appraisal of Guidelines for Research & Evaluation II (AGREE-II) instrument.[83,84] With this instrument 6 domains are assessed and an overall score of 1 (lowest quality) to 7 (best quality) is assigned. In addition to the interventions included within the scope of the HTA, some of the guidelines we identified also

included interventions outside of the scope of this HTA, notably medications, herbal supplements, and invasive treatments. Our summary focuses only on the interventions that were in the scope of this HTA.

The most recent CPG is a multidisciplinary guideline published in 2019; we rated this guideline as a "6" on the AGREE-II instrument. This guideline included a strong recommendation for CBT, a weak recommendation for hearing aids in patients with hearing loss and tinnitus, and a recommendation against rTMS.[86] The guideline panel made no recommendations on sound therapy, neuromonics, TRT, and neuromodulation therapy other than rTMS. CPGs issued by the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS; "5" on AGREE-II), and the German Association of the Scientific Medical Societies ("5" on AGREE-II) made similar recommendations for CBT.[87,88] The AAO-HNS recommended against rTMS and states that sound therapy is optional,[88] while the German society made no recommendation for or against rTMS or sound therapies but did recommend against TRT.[87] The International Federation of Clinical Neurophysiology ("4" on AGREE-II) issued guidelines specific to the use if rTMS across a wide variety of conditions, including tinnitus, in 2014. They state that low-frequency rTMS may have possible therapeutic efficacy, but results are partial and transient and many uncertainties remain.[79] Lastly, the Department of Veterans Affairs/Department of Defense issued a joint CPG in 2016 for the management of concussion and mild traumatic brain injury in 2016 that included recommendations specific to tinnitus management in this population.[85] This guideline made no recommendation for or against the use of any interventions for tinnitus in this population.

Table 10. Summary of Clinical Practice Guidelines for the Treatment of Tinnitus

Title	Year	Summary	AGREE Rating (1-worst quality to 7-best quality)
A multidisciplinary European guideline for tinnitus: diagnostics, assessment, and treatment[86]	2019	**Strong recommendation for:** CBT **Weak recommendation for:** Hearing aids for patients with hearing loss; hearing aids should not be offered to patients with tinnitus in the absence of hearing loss. **Recommendation against:** rTMS **No recommendation:** Transcranial electrical stimulation; vagus nerve stimulation; acoustic coordinated reset neuromodulation; tinnitus retraining therapy; invasive nerve stimulation, sound therapy (including masking, music, environmental sound, neuromonics)[a]	6
Association of the Scientific Medical Societies in Germany Guideline 01 7/064: Chronic Tinnitus[87]	2015	**Recommend for**: tinnitus-specific CBT (carried out using an evidence-supported and structured therapeutic manual) **Recommend against**: Tinnitus retraining therapy **No recommendation**: Sound therapy, music therapy or acoustic neuromodulation, hearing aids (although hearing aids and middle ear implants can be recommended for the treatment of an appropriate accompanying hearing loss), rTMS, other electromagnetic procedures or other electrical stimulation (e.g., transcutaneous electrical stimulation in the ear or cervical spine areas, vagus nerve stimulation)	5
American Academy of Otolaryngology-Head and Neck Surgery	2014	**Recommendation for**: CBT **Recommendation for:** Hearing aid evaluation for patients with hearing loss and persistent, bothersome tinnitus	5

Title	Year	Summary	AGREE Rating (1-worst quality to 7-best quality)
Clinical Practice Guideline: Tinnitus[88]		**Option (flexible decision making)**: Sound therapy (including environmental enrichment devices, hearing aids, ear-level sound generators, masking devices, or combination tinnitus instruments) **Recommendation against**: rTMS (for routine[b] treatment)	
International Federation of Clinical Neurophysiology: Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation[79]	2014	Low frequency (1 Hz) rTMS single or repeated sessions has possible therapeutic efficacy (Level C recommendation) but the effects are partial and transient. The best method of targeting is not fully validated and there remain numerous uncertainties about its feasibility and usefulness in clinical practice. No recommendations for high frequency rTMS.	4
VA/DoD Clinical Practice Guidelines: Management of Concussion-mild Traumatic Brain Injury[85]	2016	There is **no evidence to suggest for or against the use of any particular modality** for the treatment of tinnitus after mild traumatic brain injury. The strength of this recommendation was not assessed due to limited evidence.	5

Notes: [a] Authors state, "May be useful for acute relief purposes but is not considered an effective intervention with long-term results."
[b] Authors state, "The words routine and routinely are used to avoid setting a legal precedent and to acknowledge that there may be individual circumstances for which clinicians and patients may wish to deviate from the prescribed action in the statement."

Abbreviations: AAA = American Audiologic Association; AAO-HNSF = American Academy of Otolaryngology—Head and Neck Surgery Foundation; AGREE = Appraisal of Guidelines for Research & Evaluation II instrument; ASMS = Association of the Scientific Medical Societies (Germany); CBT = cognitive behavioral therapy; CR = coordinated reset; DoD = Department of Defense; mTBI = mild traumatic brain injury; NCRAR = National Center for Rehabilitative Auditory Research; NICE = National Institute for Health and Clinical Excellence; rTMS = repetitive transcranial magnetic stimulation; tACS = transcranial alternating current stimulation; tDCS = transcranial direct current stimulation; TRT = Tinnitus retraining therapy; VA = Department of Veterans Affairs; (t)VNS = (transcutaneous) Vagus Nerve Stimulation.

4.4 Selected Payer Coverage Policies

An overview of specific payor coverage policies for tinnitus is provided in ***Table 11***.

Table 11. Overview of Payer Coverage Policies for Tinnitus

Treatment Type	Medicare	Medicaid	Aetna	Cigna	Humana	Kaiser Permanente	Premera Blue Cross	Regence BlueShield	TRICARE	UnitedHealth
CBT	—	—	x	✓[a]	x	—	—	—	—	—
rTMS	—	—	x	x	x	—	—	x	—	x
Sound Therapy	—	—	x	—	x	x	—	—	x	x
Tinnitus-Specific Interventions	—	—	x	—	x	x	—	—	—	—

Notes: ✓ = covered when specific criteria have been met; ✕ = not covered; — = no policy identified; [a] This treatment would likely be covered on a case-by-case basis, as it pertains to moderate to severe traumatic brain injury and does not specifically address tinnitus; however, the policy specifically notes the use of CBT interventions to "address psychosocial, behavioral, and emotional impairments and to improve occupational performance."

Abbreviations: CBT = cognitive behavioral therapy; rTMS = repetitive transcranial magnetic stimulation.

Prior to 2014, a CMS National Coverage Determination (NCD) stated that tinnitus masking was considered experimental and was therefore not covered. However, effective December 18, 2014,[89] CMS removed the tinnitus NCD. As a result, there is no stated CMS policy on tinnitus treatment. Other than Cigna, which covers CBT to "address psychosocial, behavioral, and emotional impairments and to improve occupational performance," most commercial payers either do not have a specific policy or do not cover the tinnitus treatments included in the scope of this review. Specific payor coverage policies for tinnitus are detailed in ***Table 12***.

Table 12. Detailed Payer Coverage Policies for Tinnitus

Payor; Effective Date	Policy
Aetna[197] April 6, 2020	I. Aetna considers transcutaneous electrical nerve stimulation (TENS) medically necessary durable medical equipment (DME) for members with severe tinnitus when all of the following criteria are met: A. Medically correctable causes of tinnitus have been ruled out, *and* B. Member has experienced severe tinnitus for more than 6 months, *and* C. Member has tried and failed conservative tinnitus treatments, including counseling and reassurance, dietary modifications, and drug therapy. **Note**: More than 10 TENS sessions per year are not considered medically necessary for the treatment of tinnitus because of a lack of evidence that more frequent TENS treatments provides additional clinically significant benefits for this condition. II. Aetna considers tinnitus instruments (e.g., maskers, hearing aids, or combination of maskers and hearing aids) experimental and investigational for the management of members with tinnitus because the effectiveness of these instruments has not been demonstrated in randomized controlled studies with large sample size and long-term follow-up evaluation. **Note**: Tinnitus instruments such as maskers and hearing aids are approved by the Food and Drug Administration (FDA) and are classified as Class III devices; however, tinnitus masking is not approved for coverage by the Centers for Medicare &. Medicaid Services (CMS). IV. Aetna considers the following interventions experimental and investigational for the management of members with tinnitus (not an all-inclusive list): • Music therapy • Neuromonics tinnitus treatment/Neuromonics Oasis device • Noise/sound generators • Otoharmonics Levo System sound therapy • Repetitive transcranial magnetic stimulation (including continuous theta-burst stimulation) • Sequential phase shift sound cancellation treatment • Tinnitus retraining therapy • Transcranial electrical neuromodulation (e.g., alternating current stimulation, direct current stimulation, and random noise stimulation)
Cigna CBT[198] July 15, 2019 rTMS[199] March 15, 2019	**CBT: <u>Medically Necessary</u>** **An individualized program of cognitive rehabilitation is considered medically necessary for EITHER of the following:** • stroke/cerebral infarction • moderate to severe traumatic brain injury **when ALL of the following requirements are met:** • A documented cognitive impairment with related compromised functional status exists. • Neuropsychological testing or an appropriate assessment has been performed and these test or assessment results will be used in treatment planning and directing of rehabilitation strategies. • The individual is willing and able to actively participate in the treatment plan. • Significant cognitive improvement with improved related functional status is expected.

Payor; Effective Date	Policy
	American Occupational Therapy Association (AOTA): AOTA published occupational therapy practice guidelines for adults with traumatic brain injury (Wheeler et al., 2016). The recommendation for occupational therapy interventions for adults with TBI include: • Interventions to Improve Occupational Performance of People with Psychosocial, Behavioral, or Emotional Impairments ➢ Cognitive behavioral therapy (CBT) interventions to address psychosocial, behavioral, and emotional impairments and to improve occupational performance (A). **rTMS**: There have been a number of studies and meta-analyses conducted that explored the efficacy of rTMS for a selection of neuropsychiatric-related disorders. Some of the methodological limitations of these studies include small patient populations; short-term followups; variability in technique and outcome measures; and varied diagnostic groups on and off pharmacotherapy. Also, the optimal rTMS protocol have not been identified for these conditions. Therefore, the clinical utility and improvement in health outcomes of rTMS in the treatment of other psychiatric or neurological disorders have not been clearly established. rTMS has not been proven effective in the peer-reviewed published scientific literature for the following indications nor are the devices FDA approved for [tinnitus, and other medical conditions as specified in the source policy].
Humana Tinnitus Treatments[200] January 1, 2020 Transcranial Magnetic Stimulation (TMS) and Cranial Electrical Stimulation (CES)[201] January 1, 2020 Biofeedback[202] December 3, 2019	Humana members may **NOT** be eligible under the Plan for the **treatment of tinnitus** by the following modalities: • Cognitive behavioral therapy • Electrical stimulation • Hearing aids (may be excluded by contract) • Masking devices • Tinnitus retraining therapy • Repetitive transcranial magnetic stimulation (rTMS) (For information regarding coverage determination/limitations, please refer to Transcranial Magnetic Stimulation (TMS) and Cranial Electrical Stimulation (CES) Medical Coverage Policy) Humana members may **NOT** be eligible under the Plan for rTMS in **ANY** setting (e.g., ambulatory care center, health care provider office, home, hospital, outpatient facility) for any indications other than those listed above including, but may not be limited to [tinnitus, and other medical conditions as specified in the source policy]….This is considered experimental/investigational as it is not identified as widely used and generally accepted for any other proposed use as reported in nationally recognized peer-reviewed medical literature published in the English language. Humana members may **NOT** be eligible under the Plan for **biofeedback** for any indications other than those listed above including [tinnitus, and other medical conditions as specified in the source policy] … These are considered experimental/investigational as they are not identified as widely used and generally accepted for any other proposed uses as reported in nationally recognized peer-reviewed medical literature published in the English language.
Kaiser[203] 9/3/2019	The use of tinnitus masking devices for treatment of tinnitus does not meet *Kaiser Permanente Medical Technology Assessment Criteria.*
Premera Blue Cross	There are no policies regarding eligible treatments for tinnitus.
Regence Blue Shield[204] May 1, 2019	Transcranial magnetic stimulation (TMS) of the brain is considered investigational as a treatment for all other indications, including but not limited to psychiatric and neurological disorders and depression, except major depressive disorder meeting Criterion I.
Tricare[205] December 18, 1992	2.1 Medical devices may be covered when medically necessary, appropriate, the standard of care, and not otherwise excluded. 2.2 Medical devices must be FDA approved or of a type not requiring pre-market approval by the FDA. Not all of these (either FDA approved or those not requiring pre-market approval) are covered. Not all FDA-approved devices are covered. Coverage of a medical device is subject to all other requirements of the law, rules, and policy governing TRICARE. If the device is used for a noncovered or excluded indication, benefits may not be allowed. For example, tinnitus masker is an FDA-approved device; however, TRICARE considers

Payor; Effective Date	Policy
	this device unproven and, therefore, not a benefit.
UnitedHealth Transcranial Magnetic Stimulation[206] February 1, 2019 Durable Medical Equipment and Medical Supplies[207] November 19, 2019	The following are unproven and not medically necessary due to insufficient evidence of efficacy: • Transcranial magnetic stimulation for treating all medical (i.e., nonbehavioral) conditions including but not limited to [tinnitus, and other medical conditions as specified in the source policy] Tinnitus Masker: Not covered under Medicare guidelines

4.5 Limitations of This HTA

This HTA was limited to peer-reviewed studies published in English. We did not include data or results presented solely in conference abstracts. Our research questions did not include comparative effectiveness of interventions. Further, we did not include studies of neuromodulation therapies other than rTMS. We included psychological interventions other than CBT only if they were provided as part of a multicomponent intervention that typically included some version of sound therapy, which we termed 'tinnitus-specific' interventions for this HTA. We did not include studies that evaluated other forms of psychological counseling. We also did not include other kinds of non-pharmacologic interventions that might be used to treat tinnitus such as alternative and complementary therapies or lifestyle modifications. Pharmacologic treatment and invasive interventions (e.g., cochlear implants, or implantable neuromodulation devices) were also outside the scope of this review.

4.6 Ongoing Research

We identified 139 clinical trials registered in clinicaltrials.gov that are relevant to this HTA. ***Table 13*** summarizes these trials by study status and intervention category. Of these trials, the vast majority were interventional and had less than 100 subjects. A list of 35 highly relevant ongoing clinical trials by estimated primary completion date is provided in ***Appendix J, Table J1***. Additionally, our search identified 85 additional trials; of these, the majority were trials investigating drugs or alternative therapies, and a small number were focused on invasive neuromodulation treatments or dietary supplements.

Table 13. Relevant Clinical Trials by Status and Intervention Category

Study Status[a]	Sound Therapies	Neuro-modulation	Psychological or Behavioral	≥2 Types of Therapy	Etiology, Diagnosis, and Experience of Tinnitus	Total by Study Status
Not yet recruiting	4	0	1	0	1	6
Active and/or recruiting[a]	3	18	3	4	1	29
Completed	14	34	19	2	9	78

Study Status[a]	Sound Therapies	Neuro-modulation	Psychological or Behavioral	≥2 Types of Therapy	Etiology, Diagnosis, and Experience of Tinnitus	Total by Study Status
Stopped or unknown[b]	5	11	6	0	4	26
Total	26	63	29	6	15	139

Notes: [a] Includes active, not recruiting; enrolling by invitation; and recruiting. [b] Includes terminated; withdrawn; and unknown status.

Conclusion

CBT interventions, or tinnitus-specific interventions that combine psychological counseling with sound therapy may offer some benefit for reducing tinnitus-related distress and disability. Sound therapy alone and rTMS interventions in their current state may not be effective; additional research may be needed to refine these interventions. There may be few to no harms from most CBT and sound therapy interventions; the evidence is insufficient to determine harms from rTMS interventions. Evidence is lacking with respect to cost outcomes.

5. References

1. Baguley D, McFerran D, Hall D. Tinnitus. *Lancet.* 2013;382(9904):1600-1607. PMID: 23827090. doi: 10.1016/S0140-6736(13)60142-7
2. Tyler RS, Noble W, Coelho C. Considerations for the design of clinical trials for tinnitus. *Acta Otolaryngol Suppl.* 2006(556):44-49. PMID: 17114142. doi: 10.1080/03655230600895424
3. Tyler RS, Oleson J, Noble W, Coelho C, Ji H. Clinical trials for tinnitus: study populations, designs, measurement variables, and data analysis. *Prog Brain Res.* 2007;166:499-509. PMID: 17956814. doi: 10.1016/s0079-6123(07)66048-8
4. Shargorodsky J, Curhan GC, Farwell WR. Prevalence and characteristics of tinnitus among US adults. *Am J Med.* 2010;123(8):711-718. PMID: 20670725. doi: 10.1016/j.amjmed.2010.02.015
5. American Speech-Language-Hearing Association. Tinnitus and hyperacusis. https://www.asha.org/PRPSpecificTopic.aspx?folderid=8589942834&section=Incidence_and_Prevalence. Published n.d. Accessed February 14, 2020.
6. Henry JA, Roberts LE, Caspary DM, Theodoroff SM, Salvi RJ. Underlying mechanisms of tinnitus: review and clinical implications. *J Am Acad Audiol.* 2014;25(1):5-22; quiz 126. PMID: 24622858. doi: 10.3766/jaaa.25.1.2
7. Tyler RS, Baker LJ. Difficulties experienced by tinnitus sufferers. *J Speech Hear Disord.* 1983;48(2):150-154. PMID: 6621006. doi: 10.1044/jshd.4802.150
8. American Tinnitus Association. Managing your tinnitus: behavioral therapies. https://www.ata.org/managing-your-tinnitus/treatment-options/behavioral-therapies. Published 2019. Accessed November 9, 2019.
9. U.S. Food and Drug Administration. FDA permits marketing of transcranial magnetic stimulation for treatment of obsessive compulsive disorder. https://www.fda.gov/news-events/press-announcements/fda-permits-marketing-transcranial-magnetic-stimulation-treatment-obsessive-compulsive-disorder. Published 2018. Accessed February 9, 2020.
10. United Nations Development Programme. *Human development indices and indicators. 2018 statistical update.* New York, NY: United Nations Development Programme; 2018.
11. Higgins JPT, Sterne JAC, Savović J, et al. A revised tool for assessing risk of bias in randomized trials. In: Chandler J, McKenzie J, Boutron I, Welch V, eds. *Cochrane Methods.* Vol 102016. https://sites.google.com/site/riskofbiastool/welcome/rob-2-0-tool
12. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ.* 2008;336(7650):924-926. PMID: 18436948. doi: 10.1136/bmj.39489.470347.AD
13. Newman CW, Sandridge SA, Jacobson GP. Assessing Outcomes of Tinnitus Intervention. *J Am Acad Audiol.* 2014;25(1):76-105. doi: 10.3766/jaaa.25.1.6
14. Snow JB. *Tinnitus: theory and management.* Shelton, CT: PMPH-USA; 2004.

15. Schad ML, McMillan GP, Thielman EJ, et al. Comparison of acoustic therapies for tinnitus suppression: a preliminary trial. *Int J Audiol.* 2018;57(2):143-149. PMID: 29022411. doi: 10.1080/14992027.2017.1385862

16. Henry JA, McMillan G, Dann S, et al. Tinnitus Management: Randomized Controlled Trial Comparing Extended-Wear Hearing Aids, Conventional Hearing Aids, and Combination Instruments. *J Am Acad Audiol.* 2017;28(6):546-561. PMID: 28590898. doi: 10.3766/jaaa.16067

17. Li SA, Bao L, Chrostowski M. Investigating the Effects of a Personalized, Spectrally Altered Music-Based Sound Therapy on Treating Tinnitus: A Blinded, Randomized Controlled Trial. *Audiol Neurootol.* 2016;21(5):296-304. PMID: 27838685. doi: 10.1159/000450745

18. Wise K, Kobayashi K, Magnusson J, Welch D, Searchfield GD. Randomized Controlled Trial of a Perceptual Training Game for Tinnitus Therapy. *Games Health J.* 2016;5(2):141-149. PMID: 26910854. doi: 10.1089/g4h.2015.0068

19. Dineen R, Doyle J, Bench J, Perry A. The influence of training on tinnitus perception: an evaluation 12 months after tinnitus management training. *Br J Audiol.* 1999;33(1):29-51. PMID: 10219721.

20. Stein A, Wunderlich R, Lau P, et al. Clinical trial on tonal tinnitus with tailor-made notched music training. *BMC Neurol.* 2016;16:38. PMID: 26987755. doi: 10.1186/s12883-016-0558-7

21. Strauss DJ, Corona-Strauss FI, Seidler H, Haab L, Hannemann R. Notched environmental sounds: a new hearing aid-supported tinnitus treatment evaluated in 20 patients. *Clin Otolaryngol.* 2017;42(1):172-175. PMID: 26505162. doi: 10.1111/coa.12575

22. Okamoto H, Stracke H, Stoll W, Pantev C. Listening to tailor-made notched music reduces tinnitus loudness and tinnitus-related auditory cortex activity. *Proc Natl Acad Sci U S A.* 2010;107(3):1207-1210. PMID: 20080545. doi: 10.1073/pnas.0911268107

23. Hiller W, Haerkotter C. Does sound stimulation have additive effects on cognitive-behavioral treatment of chronic tinnitus? *Behav Res Ther.* 2005;43(5):595-612. PMID: 15865915. doi: 10.1016/j.brat.2004.03.012

24. Davis PB, Wilde RA, Steed LG, Hanley PJ. Treatment of tinnitus with a customized acoustic neural stimulus: a controlled clinical study. *Ear Nose Throat J.* 2008;87(6):330-339. PMID: 18561116.

25. Dineen R, Doyle J, Bench J. Managing tinnitus: a comparison of different approaches to tinnitus management training. *Br J Audiol.* 1997;31(5):331-344. PMID: 9373742.

26. Anders M, Dvorakova J, Rathova L, et al. Efficacy of repetitive transcranial magnetic stimulation for the treatment of refractory chronic tinnitus: a randomized, placebo controlled study. *Neuro Endocrinol Lett.* 2010;31(2):238-249. PMID: 20424590.

27. Barwood CH, Wilson WJ, Malicka AN, et al. The effect of rTMS on auditory processing in adults with chronic, bilateral tinnitus: a placebo-controlled pilot study. *Brain Stimul.* 2013;6(5):752-759. PMID: 23453932. doi: 10.1016/j.brs.2013.01.015

28. Chung HK, Tsai CH, Lin YC, et al. Effectiveness of theta-burst repetitive transcranial magnetic stimulation for treating chronic tinnitus. *Audiol Neurootol.* 2012;17(2):112-120. PMID: 21865723. doi: 10.1159/000330882

29. Folmer RL, Theodoroff SM, Casiana L, Shi Y, Griest S, Vachhani J. Repetitive Transcranial Magnetic Stimulation Treatment for Chronic Tinnitus: A Randomized Clinical Trial. *JAMA Otolaryngol Head Neck Surg.* 2015;141(8):716-722. PMID: 26181507. doi: 10.1001/jamaoto.2015.1219

30. Formánek M, Migaľová P, Krulová P, et al. Combined transcranial magnetic stimulation in the treatment of chronic tinnitus. *Annals of Clinical and Translational Neurology.* 2018;5(7):857-864. doi: 10.1002/acn3.587

31. Hoekstra CE, Versnel H, Neggers SF, Niesten ME, van Zanten GA. Bilateral low-frequency repetitive transcranial magnetic stimulation of the auditory cortex in tinnitus patients is not effective: a randomised controlled trial. *Audiol Neurootol.* 2013;18(6):362-373. PMID: 24157459. doi: 10.1159/000354977

32. Landgrebe M, Hajak G, Wolf S, et al. 1-Hz rTMS in the treatment of tinnitus: A sham-controlled, randomized multicenter trial. *Brain Stimul.* 2017;10(6):1112-1120. PMID: 28807845. doi: 10.1016/j.brs.2017.08.001

33. Plewnia C, Vonthein R, Wasserka B, et al. Treatment of chronic tinnitus with theta burst stimulation: a randomized controlled trial. *Neurology.* 2012;78(21):1628-1634. PMID: 22539568. doi: 10.1212/WNL.0b013e3182574ef9

34. Sahlsten H, Virtanen J, Joutsa J, et al. Electric field-navigated transcranial magnetic stimulation for chronic tinnitus: a randomized, placebo-controlled study. *Int J Audiol.* 2017;56(9):692-700. PMID: 28415897. doi: 10.1080/14992027.2017.1313461

35. Schecklmann M, Giani A, Tupak S, et al. Neuronavigated left temporal continuous theta burst stimulation in chronic tinnitus. *Restor Neurol Neurosci.* 2016;34(2):165-175. PMID: 26890094. doi: 10.3233/rnn-150518

36. Kleinjung T, Eichhammer P, Langguth B, et al. Long-term effects of repetitive transcranial magnetic stimulation (rTMS) in patients with chronic tinnitus. *Otolaryngol Head Neck Surg.* 2005;132(4):566-569. PMID: 15806046. doi: 10.1016/j.otohns.2004.09.134

37. Mennemeier M, Chelette KC, Allen S, et al. Variable changes in PET activity before and after rTMS treatment for tinnitus. *Laryngoscope.* 2011;121(4):815-822. PMID: 21287564. doi: 10.1002/lary.21425

38. Piccirillo JF, Kallogjeri D, Nicklaus J, et al. Low-frequency repetitive transcranial magnetic stimulation to the temporoparietal junction for tinnitus: four-week stimulation trial. *JAMA Otolaryngol Head Neck Surg.* 2013;139(4):388-395. PMID: 23599075. doi: 10.1001/jamaoto.2013.233

39. Piccirillo JF, Garcia KS, Nicklaus J, et al. Low-frequency repetitive transcranial magnetic stimulation to the temporoparietal junction for tinnitus. *Arch Otolaryngol Head Neck Surg.* 2011;137(3):221-228. PMID: 21422304. doi: 10.1001/archoto.2011.3

40. Plewnia C, Reimold M, Najib A, Reischl G, Plontke SK, Gerloff C. Moderate therapeutic efficacy of positron emission tomography-navigated repetitive transcranial magnetic stimulation for chronic tinnitus: a randomised, controlled pilot study. *J Neurol Neurosurg Psychiatry.* 2007;78(2):152-156. PMID: 16891384. doi: 10.1136/jnnp.2006.095612

41. Rossi S, De Capua A, Ulivelli M, et al. Effects of repetitive transcranial magnetic stimulation on chronic tinnitus: a randomised, crossover, double blind, placebo controlled study. *J Neurol Neurosurg Psychiatry.* 2007;78(8):857-863. PMID: 17314192. doi: 10.1136/jnnp.2006.105007

42. Vanneste S, De Ridder D. The involvement of the left ventrolateral prefrontal cortex in tinnitus: a TMS study. *Exp Brain Res.* 2012;221(3):345-350. PMID: 22782483. doi: 10.1007/s00221-012-3177-6

43. Vanneste S, van der Loo E, Plazier M, De Ridder D. Parietal double-cone coil stimulation in tinnitus. *Exp Brain Res.* 2012;221(3):337-343. PMID: 22782482. doi: 10.1007/s00221-012-3176-7

44. Vanneste S, Plazier M, Van de Heyning P, De Ridder D. Repetitive transcranial magnetic stimulation frequency dependent tinnitus improvement by double cone coil prefrontal stimulation. *J Neurol Neurosurg Psychiatry.* 2011;82(10):1160-1164. PMID: 21429905. doi: 10.1136/jnnp.2010.213959

45. Henry JA, Thielman EJ, Zaugg TL, et al. Telephone-Based Progressive Tinnitus Management for Persons With and Without Traumatic Brain Injury: A Randomized Controlled Trial. *Ear Hear.* 2019;40(2):227-242. PMID: 29847413. doi: 10.1097/aud.0000000000000609

46. Beukes EW, Baguley DM, Allen PM, Manchaiah V, Andersson G. Audiologist-Guided Internet-Based Cognitive Behavior Therapy for Adults With Tinnitus in the United Kingdom: A Randomized Controlled Trial. *Ear Hear.* 2018;39(3):423-433. PMID: 29095725. doi: 10.1097/aud.0000000000000505

47. Henry JA, Thielman EJ, Zaugg TL, et al. Randomized Controlled Trial in Clinical Settings to Evaluate Effectiveness of Coping Skills Education Used With Progressive Tinnitus Management. *J Speech Lang Hear Res.* 2017;60(5):1378-1397. PMID: 28418492. doi: 10.1044/2016_jslhr-h-16-0126

48. Weise C, Kleinstauber M, Andersson G. Internet-Delivered Cognitive-Behavior Therapy for Tinnitus: A Randomized Controlled Trial. *Psychosom Med.* 2016;78(4):501-510. PMID: 26867083. doi: 10.1097/psy.0000000000000310

49. Jasper K, Weise C, Conrad I, Andersson G, Hiller W, Kleinstauber M. Internet-based guided self-help versus group cognitive behavioral therapy for chronic tinnitus: a randomized controlled trial. *Psychother Psychosom.* 2014;83(4):234-246. PMID: 24970708. doi: 10.1159/000360705

50. Nyenhuis N, Zastrutzki S, Weise C, Jager B, Kroner-Herwig B. The efficacy of minimal contact interventions for acute tinnitus: a randomised controlled study. *Cogn Behav Ther.* 2013;42(2):127-138. PMID: 22413736. doi: 10.1080/16506073.2012.655305

51. Hesser H, Gustafsson T, Lunden C, et al. A randomized controlled trial of Internet-delivered cognitive behavior therapy and acceptance and commitment therapy in the

treatment of tinnitus. *J Consult Clin Psychol.* 2012;80(4):649-661. PMID: 22250855. doi: 10.1037/a0027021

52. Malouff JM, Noble W, Schutte NS, Bhullar N. The effectiveness of bibliotherapy in alleviating tinnitus-related distress. *J Psychosom Res.* 2010;68(3):245-251. PMID: 20159209. doi: 10.1016/j.jpsychores.2009.07.023

53. Robinson SK, Viirre ES, Bailey KA, et al. A randomized controlled trial of cognitive-behavior therapy for tinnitus. *Int Tinnitus J.* 2008;14(2):119-126. PMID: 19205162.

54. Weise C, Heinecke K, Rief W. Biofeedback-based behavioral treatment for chronic tinnitus: results of a randomized controlled trial. *J Consult Clin Psychol.* 2008;76(6):1046-1057. PMID: 19045972. doi: 10.1037/a0013811

55. Kaldo V, Cars S, Rahnert M, Larsen HC, Andersson G. Use of a self-help book with weekly therapist contact to reduce tinnitus distress: a randomized controlled trial. *J Psychosom Res.* 2007;63(2):195-202. PMID: 17662757. doi: 10.1016/j.jpsychores.2007.04.007

56. Sadlier M, Stephens SD, Kennedy V. Tinnitus rehabilitation: a mindfulness meditation cognitive behavioural therapy approach. *J Laryngol Otol.* 2008;122(1):31-37. PMID: 17451612. doi: 10.1017/s0022215107007438

57. Andersson G, Porsaeus D, Wiklund M, Kaldo V, Larsen HC. Treatment of tinnitus in the elderly: a controlled trial of cognitive behavior therapy. *Int J Audiol.* 2005;44(11):671-675. PMID: 16379495.

58. Zachriat C, Kroner-Herwig B. Treating chronic tinnitus: comparison of cognitive-behavioural and habituation-based treatments. *Cogn Behav Ther.* 2004;33(4):187-198. PMID: 15625793. doi: 10.1080/16506070410029568

59. Kroner-Herwig B, Frenzel A, Fritsche G, Schilkowsky G, Esser G. The management of chronic tinnitus: comparison of an outpatient cognitive-behavioral group training to minimal-contact interventions. *J Psychosom Res.* 2003;54(4):381-389. PMID: 12670617. doi: 10.1016/s0022-3999(02)00400-2

60. Andersson G, Stromgren T, Strom L, Lyttkens L. Randomized controlled trial of internet-based cognitive behavior therapy for distress associated with tinnitus. *Psychosom Med.* 2002;64(5):810-816. PMID: 12271112. doi: 10.1097/01.psy.0000031577.42041.f8

61. Martz E, Chesney MA, Livneh H, Jelleberg C, Fuller B, Henry JA. A pilot randomized clinical trial comparing three brief group interventions for individuals with tinnitus. *Glob Adv Health Med.* 2018;7:2164956118783659. PMID: 30013820. doi: 10.1177/2164956118783659

62. Henry JL, Wilson PH. The Psychological Management of Tinnitus: Comparison of a Combined Cognitive Educational Program, Education Alone and a Waiting-List Control. *Int Tinnitus J.* 1996;2:9-20. PMID: 10753339.

63. Henry JL, Wilson PH. An evaluation of two types of cognitive intervention in the management of chronic tinnitus. *Scand J Behav Ther.* 1998;27(4):156-166.

64. Abbott JA, Kaldo V, Klein B, et al. A cluster randomised trial of an internet-based intervention program for tinnitus distress in an industrial setting. *Cogn Behav Ther.* 2009;38(3):162-173. PMID: 19675959. doi: 10.1080/16506070902763174

65. Zenner HP, Vonthein R, Zenner B, et al. Standardized tinnitus-specific individual cognitive-behavioral therapy: a controlled outcome study with 286 tinnitus patients. *Hear Res.* 2013;298:117-125. PMID: 23287811. doi: 10.1016/j.heares.2012.11.013

66. Thomsen J, Bretlau P, Tos M, Johnsen NJ. Meniere's disease: endolymphatic sac decompression compared with sham (placebo) decompression. *Ann N Y Acad Sci.* 1981;374:820-830. PMID: 7041752. doi: 10.1111/j.1749-6632.1981.tb30922.x

67. Henry JA, Stewart BJ, Griest S, Kaelin C, Zaugg TL, Carlson K. Multisite Randomized Controlled Trial to Compare Two Methods of Tinnitus Intervention to Two Control Conditions. *Ear Hear.* 2016;37(6):e346-e359. PMID: 27438870. doi: 10.1097/aud.0000000000000330

68. Cima RF, Maes IH, Joore MA, et al. Specialised treatment based on cognitive behaviour therapy versus usual care for tinnitus: a randomised controlled trial. *Lancet.* 2012;379(9830):1951-1959. PMID: 22633033. doi: 10.1016/s0140-6736(12)60469-3

69. Westin VZ, Schulin M, Hesser H, et al. Acceptance and commitment therapy versus tinnitus retraining therapy in the treatment of tinnitus: a randomised controlled trial. *Behav Res Ther.* 2011;49(11):737-747. PMID: 21864830. doi: 10.1016/j.brat.2011.08.001

70. Seydel C, Haupt H, Szczepek AJ, Klapp BF, Mazurek B. Long-term improvement in tinnitus after modified tinnitus retraining therapy enhanced by a variety of psychological approaches. *Audiol Neurootol.* 2010;15(2):69-80. PMID: 19657182. doi: 10.1159/000231632

71. Henry JA, Loovis C, Montero M, et al. Randomized clinical trial: group counseling based on tinnitus retraining therapy. *J Rehabil Res Dev.* 2007;44(1):21-32. PMID: 17551855.

72. Caffier PP, Haupt H, Scherer H, Mazurek B. Outcomes of long-term outpatient tinnitus-coping therapy: psychometric changes and value of tinnitus-control instruments. *Ear Hear.* 2006;27(6):619-627. PMID: 17086074. doi: 10.1097/01.aud.0000240504.77861.1a

73. Bauer CA, Berry JL, Brozoski TJ. The effect of tinnitus retraining therapy on chronic tinnitus: a controlled trial. *Laryngoscope Investig Otolaryngol.* 2017;2(4):166-177. PMID: 28894836. doi: 10.1002/lio2.76

74. Krick CM, Grapp M, Daneshvar-Talebi J, Reith W, Plinkert PK, Bolay HV. Cortical reorganization in recent-onset tinnitus patients by the Heidelberg Model of Music Therapy. *Front Neurosci.* 2015;9:49. PMID: 25745385. doi: 10.3389/fnins.2015.00049

75. Teismann H, Okamoto H, Pantev C. Short and intense tailor-made notched music training against tinnitus: the tinnitus frequency matters. *PLoS One.* 2011;6(9):e24685. PMID: 21935438. doi: 10.1371/journal.pone.0024685

76. Pichora-Fuller MK, Santaguida P, Hammill A, et al. Evaluation and Treatment of Tinnitus: Comparative Effectiveness. *Evaluation and Treatment of Tinnitus: Comparative Effectiveness*. Rockville (MD)2013. 24049842

77. Hoare DJ, Edmondson-Jones M, Sereda M, Akeroyd MA, Hall D. Amplification with hearing aids for patients with tinnitus and co-existing hearing loss. *Cochrane Database Syst Rev.* 2014(1):Cd010151. PMID: 24482186. doi: 10.1002/14651858.CD010151.pub2

78. Meng Z, Liu S, Zheng Y, Phillips JS. Repetitive transcranial magnetic stimulation for tinnitus. *Cochrane Database of Systematic Reviews.* 2011(10). PMID: CD007946. doi: 10.1002/14651858.CD007946.pub2

79. Lefaucheur JP, Aleman A, Baeken C, et al. Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS): An update (2014-2018). *Clin Neurophysiol.* 2020;131(2):474-528. PMID: 31901449. doi: 10.1016/j.clinph.2019.11.002

80. Londero A, Bonfils P, Lefaucheur JP. Transcranial magnetic stimulation and subjective tinnitus. A review of the literature, 2014-2016. *Eur Ann Otorhinolaryngol Head Neck Dis.* 2018;135(1):51-58. PMID: 29287622. doi: 10.1016/j.anorl.2017.12.001

81. Martinez-Devesa P, Perera R, Theodoulou M, Waddell A. Cognitive behavioural therapy for tinnitus. *Cochrane Database of Systematic Reviews.* 2010(9). PMID: CD005233. doi: 10.1002/14651858.CD005233.pub3

82. Phillips JS, McFerran D. Tinnitus Retraining Therapy (TRT) for tinnitus. *Cochrane Database Syst Rev.* 2010(3):Cd007330. PMID: 20238353. doi: 10.1002/14651858.CD007330.pub2

83. AGREE Next Steps Consortium. The AGREE II Instrument [Electronic Version]. http://www.agreetrust.org. Published 2017. Accessed January 15, 2020.

84. Brouwers MC, Kho ME, Browman GP, et al. AGREE II: Advancing guideline development, reporting and evaluation in health care. *CMAJ.* 2010;182(18):E839-842. PMID: 20603348. doi: 10.1503/cmaj.090449

85. The Management of Concussion-mild Traumatic Brain Injury Working Group. VA/DoD clinical practice guidelines. Management of concussion-mild traumatic brain injury (mTBI). https://www.healthquality.va.gov/guidelines/Rehab/mtbi/. Published 2016. Updated September 28, 2017. Accessed February 20, 2020.

86. Cima RFF, Mazurek B, Haider H, et al. A multidisciplinary European guideline for tinnitus: diagnostics, assessment, and treatment. *HNO.* 2019;67(Suppl 1):10-42. PMID: 30847513. doi: 10.1007/s00106-019-0633-7

87. German Society of Otorhinolaryngology and Head and Neck Surgery. *German S3 guideline Ol 7/064: chronic tinnitus* 2015.

88. Tunkel DE, Bauer CA, Sun GH, et al. Clinical practice guideline: tinnitus. *Otolaryngol Head Neck Surg.* 2014;151(2 Suppl):S1-S40. PMID: 25273878. doi: 10.1177/0194599814545325

89. Centers for Medicare & Medicaid Services. National Coverage Determination (NCD) for Tinnitus Masking - RETIRED (50.6). https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=85&ncdver=2&MCDIndexType=7&mcdtypename=Expedited+Pro

cess+to+Remove+National+Coverage+Determinations&bc=AAAAQAAABAAA&. Published 2014. Accessed February 9, 2020.

90. Tyler R, Coelho C, Tao P, et al. Identifying tinnitus subgroups with cluster analysis. *Am J Audiol.* 2008;17(2):S176-184. PMID: 19056922. doi: 10.1044/1059-0889(2008/07-0044)

91. Nondahl DM, Cruickshanks KJ, Wiley TL, et al. The ten-year incidence of tinnitus among older adults. *Int J Audiol.* 2010;49(8):580-585. PMID: 20560859. doi: 10.3109/14992021003753508

92. Bhatt JM, Lin HW, Bhattacharyya N. Prevalence, Severity, Exposures, and Treatment Patterns of Tinnitus in the United States. *JAMA Otolaryngol Head Neck Surg.* 2016;142(10):959-965. PMID: 27441392. doi: 10.1001/jamaoto.2016.1700

93. Ziai K, Moshtaghi O, Mahboubi H, Djalilian HR. Tinnitus Patients Suffering from Anxiety and Depression: A Review. *Int Tinnitus J.* 2017;21(1):68-73. PMID: 28723605. doi: 10.5935/0946-5448.20170013

94. Pinto PC, Marcelos CM, Mezzasalma MA, Osterne FJ, de Melo Tavares de Lima MA, Nardi AE. Tinnitus and its association with psychiatric disorders: systematic review. *J Laryngol Otol.* 2014;128(8):660-664. PMID: 25033303. doi: 10.1017/s0022215114001030

95. Bhatt JM, Bhattacharyya N, Lin HW. Relationships between tinnitus and the prevalence of anxiety and depression. *Laryngoscope.* 2017;127(2):466-469. PMID: 27301552. doi: 10.1002/lary.26107

96. Szibor A, Makitie A, Aarnisalo AA. Tinnitus and suicide: An unresolved relation. *Audiol Res.* 2019;9(1):222. PMID: 31275536. doi: 10.4081/audiores.2019.222

97. Aazh H, Moore BCJ. Thoughts about Suicide and Self-Harm in Patients with Tinnitus and Hyperacusis. *J Am Acad Audiol.* 2018;29(3):255-261. PMID: 29488875. doi: 10.3766/jaaa.16181

98. Cronlein T, Langguth B, Pregler M, Kreuzer PM, Wetter TC, Schecklmann M. Insomnia in patients with chronic tinnitus: Cognitive and emotional distress as moderator variables. *J Psychosom Res.* 2016;83:65-68. PMID: 27020079. doi: 10.1016/j.jpsychores.2016.03.001

99. Asplund R. Sleepiness and sleep in elderly persons with tinnitus. *Arch Gerontol Geriatr.* 2003;37(2):139-145. PMID: 12888227.

100. Folmer RL, Griest SE. Tinnitus and insomnia. *Am J Otolaryngol.* 2000;21(5):287-293. PMID: 11032291. doi: 10.1053/ajot.2000.9871

101. Wallhausser-Franke E, Schredl M, Delb W. Tinnitus and insomnia: is hyperarousal the common denominator? *Sleep Med Rev.* 2013;17(1):65-74. PMID: 22750224. doi: 10.1016/j.smrv.2012.04.003

102. Tyler RS, Aran JM, Dauman R. Recent Advances in Tinnitus. *Am J Audiol.* 1992;1(4):36-44. PMID: 26660130. doi: 10.1044/1059-0889.0104.36

103. Maes IH, Cima RF, Vlaeyen JW, Anteunis LJ, Joore MA. Tinnitus: a cost study. *Ear Hear.* 2013;34(4):508-514. PMID: 23411656. doi: 10.1097/AUD.0b013e31827d113a

104. Goldstein E, Ho CX, Hanna R, et al. Cost of care for subjective tinnitus in relation to patient satisfaction. *Otolaryngol Head Neck Surg.* 2015;152(3):518-523. PMID: 25632027. doi: 10.1177/0194599814566179

105. Hoare DJ, Searchfield GD, El Refaie A, Henry JA. Sound therapy for tinnitus management: practicable options. *J Am Acad Audiol.* 2014;25(1):62-75. PMID: 24622861. doi: 10.3766/jaaa.25.1.5

106. Vanneste S, De Ridder D. Noninvasive and invasive neuromodulation for the treatment of tinnitus: an overview. *Neuromodulation.* 2012;15(4):350-360. PMID: 22494273. doi: 10.1111/j.1525-1403.2012.00447.x

107. Peter N, Kleinjung T. Neuromodulation for tinnitus treatment: an overview of invasive and non-invasive techniques. *J Zhejiang Univ Sci B.* 2019;20(2):116-130. PMID: 29770647. doi: 10.1631/jzus.B1700117

108. Sweetow RW. Cognitive-behavior modification. In: Tyler R, ed. *Tinnitus handbook*: Singular Publishing Group; 2000:297-311.

109. Jastreboff PJ, Jastreboff M. Tinnitus retraining therapy: an update. https://www.audiologyonline.com/articles/tinnitus-retraining-therapy-an-update-1286. Published 2000. Accessed November 9, 2019.

110. UCSF Health. Neuromonics. https://www.ucsfhealth.org/treatments/neuromonics/. Published. Accessed 10/9/2019, 2019.

111. Davis PB, Paki B, Hanley PJ. Neuromonics Tinnitus Treatment: third clinical trial. *Ear Hear.* 2007;28(2):242-259. PMID: 17496674. doi: 10.1097/AUD.0b013e3180312619

112. Tyler R, Gehringer AK, Noble W, Dunn CC, Witt SA, Bardia A. Tinnitus Activities Treatment. In: Tyler RS, ed. *Tinnitus Treatment: Clinical Protocols*. New York, NY: Thieme 2006:116-132.

113. Henry JA, Zaugg TL, Myers PJ, Kendall CJ. *Progressive Tinnitus Management Clinical Handbook for Audiologists.* Long Beach, CA VA Employee Education System; 2019. https://www.ncrar.research.va.gov/Education/Documents/TinnitusDocuments/00_HenryPTM-HB_i-xviFM-LK.pdf

114. U.S. Food and Drug Administration. 510(k) Premarket Notification. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?start_search=1&Center=&Panel=&ProductCode=KLW&KNumber=&Applicant=&DeviceName=&Type=&ThirdPartyReviewed=&ClinicalTrials=&Decision=&DecisionDateFrom=&DecisionDateTo=08%2F21%2F2019&IVDProducts=&Redact510K=&CombinationProducts=&ZNumber=&PAGENUM=500. Published 2019. Accessed September 3, 2019.

115. U.S. Food and Drug Administration. Class II special controls guidance document: repetitive transcranial magnetic stimulation (rTMS) systems - guidance for industry and FDA staff https://www.fda.gov/regulatory-information/search-fda-guidance-documents/class-ii-special-controls-guidance-document-repetitive-transcranial-magnetic-stimulation-rtms. Published 2018. Accessed February 9, 2020.

116. Berkman ND, Lohr KN, Ansari MT, et al. Grading the strength of a body of evidence when assessing health care interventions: An EPC update. *J Clin Epidemiol.* 2014;68(11):1312-1324. PMID: 25721570. doi: 10.1016/j.jclinepi.2014.11.023

117. Guyatt GH, Oxman AD, Kunz R, et al. GRADE guidelines 6. Rating the quality of evidence--imprecision. *J Clin Epidemiol.* 2011;64(12):1283-1293. PMID: 21839614. doi: 10.1016/j.jclinepi.2011.01.012

118. Freedland KE, Mohr DC, Davidson KW, Schwartz JE. Usual and unusual care: existing practice control groups in randomized controlled trials of behavioral interventions. *Psychosom Med.* 2011;73(4):323-335. PMID: 21536837. doi: 10.1097/PSY.0b013e318218e1fb

119. Newman CW, Jacobson GP, Spitzer JB. Development of the Tinnitus Handicap Inventory. *Arch Otolaryngol Head Neck Surg.* 1996;122(2):143-148. PMID: 8630207. doi: 10.1001/archotol.1996.01890140029007

120. Baguley DM, Andersson G. Factor analysis of the Tinnitus Handicap Inventory. *Am J Audiol.* 2003;12(1):31-34. PMID: 12894865. doi: 10.1044/1059-0889(2003/007)

121. Zeman F, Koller M, Schecklmann M, Langguth B, Landgrebe M. Tinnitus assessment by means of standardized self-report questionnaires: psychometric properties of the Tinnitus Questionnaire (TQ), the Tinnitus Handicap Inventory (THI), and their short versions in an international and multi-lingual sample. *Health Qual Life Outcomes.* 2012;10:128. PMID: 23078754. doi: 10.1186/1477-7525-10-128

122. Newman CW, Sandridge SA, Jacobson GP. Psychometric adequacy of the Tinnitus Handicap Inventory (THI) for evaluating treatment outcome. *J Am Acad Audiol.* 1998;9(2):153-160. PMID: 9564679.

123. Zeman F, Koller M, Figueiredo R, et al. Tinnitus handicap inventory for evaluating treatment effects: which changes are clinically relevant? *Otolaryngol Head Neck Surg.* 2011;145(2):282-287. PMID: 21493265. doi: 10.1177/0194599811403882

124. Hallam RS, Jakes SC, Hinchcliffe R. Cognitive variables in tinnitus annoyance. *Br J Clin Psychol.* 1988;27(3):213-222. PMID: 3191301. doi: 10.1111/j.2044-8260.1988.tb00778.x

125. Goebel G, Hiller W. [The tinnitus questionnaire. A standard instrument for grading the degree of tinnitus. Results of a multicenter study with the tinnitus questionnaire]. *Hno.* 1994;42(3):166-172. PMID: 8175381.

126. Adamchic I, Tass PA, Langguth B, et al. Linking the Tinnitus Questionnaire and the subjective Clinical Global Impression: which differences are clinically important? *Health Qual Life Outcomes.* 2012;10:79. PMID: 22781703. doi: 10.1186/1477-7525-10-79

127. Hiller W, Goebel G. Rapid assessment of tinnitus-related psychological distress using the Mini-TQ. *Int J Audiol.* 2004;43(10):600-604. PMID: 15724525.

128. Newman CW, Wharton JA, Jacobson GP. Retest stability of the tinnitus handicap questionnaire. *Ann Otol Rhinol Laryngol.* 1995;104(9 Pt 1):718-723. PMID: 7661523. doi: 10.1177/000348949510400910

129. Kuk FK, Tyler RS, Russell D, Jordan H. The psychometric properties of a tinnitus handicap questionnaire. *Ear Hear.* 1990;11(6):434-445. PMID: 2073977. doi: 10.1097/00003446-199012000-00005

130. Kennedy V, Wilson C, Stephens D. Quality of life and tinnitus. *Audiological Medicine.* 2004;2(1):29-40. doi: 10.1080/16513860410027349

131. Wilson PH, Henry J, Bowen M, Haralambous G. Tinnitus reaction questionnaire: psychometric properties of a measure of distress associated with tinnitus. *J Speech Hear Res.* 1991;34(1):197-201. PMID: 2008074.

132. Meikle MB, Henry JA, Griest SE, et al. The tinnitus functional index: development of a new clinical measure for chronic, intrusive tinnitus. *Ear Hear.* 2012;33(2):153-176. PMID: 22156949. doi: 10.1097/AUD.0b013e31822f67c0

133. Fackrell K, Hall DA, Barry JG, Hoare DJ. Psychometric properties of the Tinnitus Functional Index (TFI): Assessment in a UK research volunteer population. *Hear Res.* 2016;335:220-235. PMID: 2016-22395-022. doi: 10.1016/j.heares.2015.09.009

134. Fackrell K, Hall DA, Barry JG, Hoare DJ. Performance of the Tinnitus Functional Index as a diagnostic instrument in a UK clinical population. *Hear Res.* 2017. PMID: 29129348. doi: 10.1016/j.heares.2017.10.016

135. Adamchic I, Langguth B, Hauptmann C, Tass PA. Psychometric evaluation of visual analog scale for the assessment of chronic tinnitus. *Am J Audiol.* 2012;21(2):215-225. PMID: 22846637. doi: 10.1044/1059-0889(2012/12-0010)

136. Jakes SC, Hallam RS, Chambers C, Hinchcliffe R. A factor analytical study of tinnitus complaint behaviour. *Audiology.* 1985;24(3):195-206. PMID: 4004646. doi: 10.3109/00206098509070103

137. Jakes S, Hallam R, McKenna L, Hinchcliffe R. Group cognitive therapy for medical patients: an application to tinnitus. *Cognit Ther Res.* 1992;16(1):67-82.

138. Wilson PH, Henry JL. Tinnitus cognitions questionnaire: development and psychometric properties of a measure of dysfunctional cognitions associated with tinnitus. *Int Tinnitus J.* 1998;4(1):23-30. PMID: 10753381.

139. Dillmann U, Nilges P, Saile H, Gerbershagen H. Behinderungseinsch??tzung bei chronischen Schmerzpatienten. *Der Schmerz.* 1994;8:100-110. doi: 10.1007/BF02530415

140. Budd RJ, Pugh R. Tinnitus coping style and its relationship to tinnitus severity and emotional distress. *J Psychosom Res.* 1996;41(4):327-335. PMID: 8971662. doi: 10.1016/s0022-3999(96)00171-7

141. Budd RJ, Pugh R. The relationship between coping style, tinnitus severity and emotional distress in a group of tinnitus sufferers. *Br J Health Psychol.* 1996;1(3):219-229.

142. Meikle MB, Griest SE, Stewart BJ, Press LS. Measuring the negative impact of tinnitus: a brief severity index. Midwinter Meeting: Association for Research in Otolaryngology; Feb 5–9, 1995; St. Petersburg Beach, FL.

143. Westin V, Hayes SC, Andersson G. Is it the sound or your relationship to it? The role of acceptance in predicting tinnitus impact. *Behav Res Ther.* 2008;46(12):1259-1265. PMID: 18926522. doi: 10.1016/j.brat.2008.08.008

144. Weise C, Kleinstauber M, Hesser H, Westin VZ, Andersson G. Acceptance of tinnitus: validation of the tinnitus acceptance questionnaire. *Cogn Behav Ther.* 2013;42(2):100-115. PMID: 23627873. doi: 10.1080/16506073.2013.781670

145. Meikle MB, Stewart BJ, Griest SE, et al. Assessment of tinnitus: measurement of treatment outcomes. *Prog Brain Res.* 2007;166:511-521. PMID: 17956815. doi: 10.1016/s0079-6123(07)66049-x

146. Sweetow R, Levy M. Tinnitus severity scaling for diagnostic/therapeutic usage. *Hear Instrum.* 1990;41(20-21):46.

147. Fackrell K, Hoare D. Questionnaires to measure tinnitus severity *ENT & Audiol News.* 2014;22(6).

148. Ferguson CJ. An effect size primer: a guide for clinicians and researchers. *Prof Psychol Res Pr.* 2009;40(5):532-538. doi: 10.1037/a0015808

149. Sawilowsky SS. New effect size rules of thumb. *J Mod Appl Stat Methods.* 2009;8(2):26.

150. Cohen J. *Statistical power analysis for the behavioral sciences.* 2nd ed. New York, NY: Routledge; 2013.

151. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand.* 1983;67(6):361-370. PMID: 6880820. doi: 10.1111/j.1600-0447.1983.tb09716.x

152. Lemay KR, Tulloch HE, Pipe AL, Reed JL. Establishing the Minimal Clinically Important Difference for the Hospital Anxiety and Depression Scale in Patients With Cardiovascular Disease. *J Cardiopulm Rehabil Prev.* 2019;39(6):E6-e11. PMID: 30489438. doi: 10.1097/hcr.0000000000000379

153. Beck AT, Steer RA, Ball R, Ranieri W. Comparison of Beck Depression Inventories -IA and -II in psychiatric outpatients. *J Pers Assess.* 1996;67(3):588-597. PMID: 8991972. doi: 10.1207/s15327752jpa6703_13

154. Button KS, Kounali D, Thomas L, et al. Minimal clinically important difference on the Beck Depression Inventory--II according to the patient's perspective. *Psychol Med.* 2015;45(15):3269-3279. PMID: 26165748. doi: 10.1017/s0033291715001270

155. Masson SC, Tejani AM. Minimum clinically important differences identified for commonly used depression rating scales. *J Clin Epidemiol.* 2013;66(7):805-807. PMID: 23618794. doi: 10.1016/j.jclinepi.2013.01.010

156. Hamilton M. The assessment of anxiety states by rating. *Br J Med Psychol.* 1959;32(1):50-55. PMID: 13638508. doi: 10.1111/j.2044-8341.1959.tb00467.x

157. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry.* 1960;23(1):56-62. PMID: 14399272. doi: 10.1136/jnnp.23.1.56

158. Bagby RM, Ryder AG, Schuller DR, Marshall MB. The Hamilton Depression Rating Scale: has the gold standard become a lead weight? *Am J Psychiatry.* 2004;161(12):2163-2177. PMID: 15569884. doi: 10.1176/appi.ajp.161.12.2163

159. Meyer TD, Hautzinger M. Allgemeine Depressions-Skala (ADS). Normierung an Minderjährigen und Erweiterung zur Erfassung manischer Symptome (ADMS). *Diagnostica.* 2001.

160. Reiss S, Peterson RA, Gursky DM, McNally RJ. Anxiety sensitivity, anxiety frequency and the prediction of fearfulness. *Behav Res Ther.* 1986;24(1):1-8. PMID: 3947307. doi: 10.1016/0005-7967(86)90143-9

161. Lovibond SH, Lovibond PF. *Manual for depression, anxiety and stress scales.* Sydney: Psychological Foundation of Australia; 1995.

162. Psychology Foundation of Australia. Depression anxiety stress scales (DASS). http://www2.psy.unsw.edu.au/dass/. Published 2018. Accessed February 13, 2020.

163. Spitzer RL, Kroenke K, Williams JB, Lowe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med.* 2006;166(10):1092-1097. PMID: 16717171. doi: 10.1001/archinte.166.10.1092

164. Lowe B, Decker O, Muller S, et al. Validation and standardization of the Generalized Anxiety Disorder Screener (GAD-7) in the general population. *Med Care.* 2008;46(3):266-274. PMID: 18388841. doi: 10.1097/MLR.0b013e318160d093

165. Derogatis LR, Fitzpatrick M. The SCL-90-R, the Brief Symptom Inventory (BSI), and the BSI-18. In: Maruish ME, ed. *The use of psychological testing for treatment planning and outcomes assessment: Instruments for adults*. New Jersey: Lawrence Erlbaum Associates Publishers; 2004:1-41.

166. Derogatis LR. Symptom Checklist-90-Revised (SCL-90-R) https://www.pearsonassessments.com/store/usassessments/en/Store/Professional-Assessments/Personality-%26-Biopsychosocial/Symptom-Checklist-90-Revised/p/100000645.html?tab=product-details. Published 1994. Accessed February 9, 2020.

167. Goldberg DP, Blackwell B. Psychiatric illness in general practice. A detailed study using a new method of case identification. *Br Med J.* 1970;1(5707):439-443. PMID: 5420206. doi: 10.1136/bmj.2.5707.439

168. Cohen S, Janicki-Deverts D. Who's stressed? Distributions of psychological stress in the United States in probability samples from 1983, 2006, and 2009 1. *J Appl Soc Psychol.* 2012;42(6):1320-1334.

169. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. *J Health Soc Behav.* 1983;24(4):385-396. PMID: 6668417.

170. Eskildsen A, Dalgaard VL, Nielsen KJ, et al. Cross-cultural adaptation and validation of the Danish consensus version of the 10-item Perceived Stress Scale. *Scand J Work Environ Health.* 2015:486-490.

171. Derogatis LR. The Derogatis stress profile (DSP): Quantification of psychological stress. *Research paradigms in psychosomatic medicine.* Vol 17: Karger Publishers; 1987:30-54.

172. Derogatis LR. Derogatis Stress Profile (DSP®). http://www.derogatis-tests.com/dsp_synopsis.asp. Published 1980. Accessed February 9, 2020.

173. Fliege H, Rose M, Arck P, et al. The Perceived Stress Questionnaire (PSQ) reconsidered: validation and reference values from different clinical and healthy adult samples. *Psychosom Med.* 2005;67(1):78-88. PMID: 15673628. doi: 10.1097/01.psy.0000151491.80178.78

174. Carver CS, Scheier MF, Weintraub JK. Assessing coping strategies: a theoretically based approach. *J Pers Soc Psychol.* 1989;56(2):267-283. PMID: 2926629. doi: 10.1037//0022-3514.56.2.267

175. Folkman S, Lazarus RS, Gruen RJ, DeLongis A. Appraisal, coping, health status, and psychological symptoms. *J Pers Soc Psychol.* 1986;50(3):571-579. PMID: 3701593. doi: 10.1037//0022-3514.50.3.571

176. Vitaliano PP, Russo J, Carr JE, Maiuro RD, Becker J. The ways of coping checklist: revision and psychometric properties. *Multivariate Behav Res.* 1985;20(1):3-26. PMID: 26776273. doi: 10.1207/s15327906mbr2001_1

177. Bastien CH, Vallières A, Morin CM. Validation of the Insomnia Severity Index as an outcome measure for insomnia research. *Sleep medicine.* 2001;2(4):297-307.

178. Yang M, Morin C, Schaefer K, Wallenstein G. Interpreting score differences in the Insomnia Severity Index: Using health-related outcomes to define the minimally important difference. *Curr Med Res Opin.* 2009;25:2487-2494. doi: 10.1185/03007990903167415

179. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep.* 1991;14(6):540-545. PMID: 1798888. doi: 10.1093/sleep/14.6.540

180. Johns MW. The Epworth Sleepiness Scale. About the ESS. https://epworthsleepinessscale.com/about-the-ess/. Published 1990. Accessed February 9, 2020.

181. Jenkins CD, Stanton BA, Niemcryk SJ, Rose RM. A scale for the estimation of sleep problems in clinical research. *J Clin Epidemiol.* 1988;41(4):313-321. PMID: 3351539. doi: 10.1016/0895-4356(88)90138-2

182. Development of the World Health Organization WHOQOL-BREF quality of life assessment. The WHOQOL Group. *Psychol Med.* 1998;28(3):551-558. PMID: 9626712. doi: 10.1017/s0033291798006667

183. Frisch MB, Cornell J, Villanueva M, Retzlaff PJ. Clinical validation of the Quality of Life Inventory. A measure of life satisfaction for use in treatment planning and outcome assessment. *Psychol Assess.* 1992;4(1):92.

184. Ware J, Ma K, Keller SD. SF-36 physical and mental health summary scales: a user's manual. https://www.researchgate.net/profile/John_Ware/publication/292390260_SF-36_Physical_and_Mental_Health_Summary_Scales_a_User%27s_Manual/links/5af580264585157136caee31/SF-36-Physical-and-Mental-Health-Summary-Scales-a-Users-Manual.pdf?origin=publication_detail. Published 1994. Accessed February 9, 2020.

185. Jayadevappa R, Cook R, Chhatre S. Minimal important difference to infer changes in health-related quality of life-a systematic review. *J Clin Epidemiol.* 2017;89:188-198. PMID: 28676426. doi: 10.1016/j.jclinepi.2017.06.009

186. Feeny D, Furlong W, Torrance GW, et al. Multiattribute and single-attribute utility functions for the health utilities index mark 3 system. *Med Care.* 2002;40(2):113-128. PMID: 11802084. doi: 10.1097/00005650-200202000-00006

187. Busner J, Targum SD. The clinical global impressions scale: applying a research tool in clinical practice. *Psychiatry (Edgmont (Pa. : Township)).* 2007;4(7):28-37. PMID: 20526405.

188. Spaans HP, Verwijk E, Stek ML, et al. Early Complete Remitters After Electroconvulsive Therapy: Profile and Prognosis. *J ect.* 2016;32(2):82-87. PMID: 26796500. doi: 10.1097/yct.0000000000000298

189. Henry JA, Frederick M, Sell S, Griest S, Abrams H. Validation of a novel combination hearing aid and tinnitus therapy device. *Ear Hear.* 2015;36(1):42-52. PMID: 25211767. doi: 10.1097/aud.0000000000000093

190. Dineen R, Doyle J, Bench J. Audiological and psychological characteristics of a group of tinnitus sufferers, prior to tinnitus management training. *Br J Audiol.* 1997;31(1):27-38. PMID: 9056041.

191. Langguth B, Kleinjung T, Marienhagen J, et al. Transcranial magnetic stimulation for the treatment of tinnitus: effects on cortical excitability. *BMC Neurosci.* 2007;8:45. PMID: 17605764. doi: 10.1186/1471-2202-8-45

192. Beukes EW, Allen PM, Baguley DM, Manchaiah V, Andersson G. Long-term efficacy of audiologist-guided internet-based cognitive behavior therapy for tinnitus. *Am J Audiol.* 2018;27(3s):431-447. PMID: 30452747. doi: 10.1044/2018_aja-imia3-18-0004

193. Conrad I, Kleinstauber M, Jasper K, Hiller W, Andersson G, Weise C. The changeability and predictive value of dysfunctional cognitions in cognitive behavior therapy for chronic tinnitus. *Int J Behav Med.* 2015;22(2):239-250. PMID: 25031187. doi: 10.1007/s12529-014-9425-3

194. Maes IH, Cima RF, Anteunis LJ, et al. Cost-effectiveness of specialized treatment based on cognitive behavioral therapy versus usual care for tinnitus. *Otol Neurotol.* 2014;35(5):787-795. PMID: 24829038. doi: 10.1097/mao.0000000000000331

195. Sereda M, Xia J, El Refaie A, Hall DA, Hoare DJ. Sound therapy (using amplification devices and/or sound generators) for tinnitus. *Cochrane Database Syst Rev.* 2018;12:Cd013094. PMID: 30589445. doi: 10.1002/14651858.CD013094.pub2

196. Schoisswohl S, Agrawal K, Simoes J, et al. RTMS parameters in tinnitus trials: a systematic review. *Sci Rep.* 2019;9(1):12190. PMID: 31434985. doi: 10.1038/s41598-019-48750-9

197. Aetna. Tinnitus treatments. http://www.aetna.com/cpb/medical/data/400_499/0406.html. Published 2019. Accessed February 9, 2020.

198. Cigna. Cigna medical coverage policy- therapy services cognitive rehabilitation. https://cignaforhcp.cigna.com/public/content/pdf/coveragePolicies/medical/CPG270_cognitive_rehab.pdf. Published 2019. Accessed February 9, 2020.

199. Cigna. Cigna medical coverage policy. Transcranial magnetic stimulation. https://cignaforhcp.cigna.com/public/content/pdf/coveragePolicies/medical/mm_0383_co

veragepositioncriteria_transcranial_magnetic_stimulation.pdf. Published 2019. Accessed February 9, 2020.

200. Humana. Tinnitus treatments. Medical coverage policy. http://apps.humana.com/tad/tad_new/Search.aspx?criteria=Tinnitus&searchtype=freetext&policyType=both. Published 2020. Accessed February 20, 2020.

201. Humana. Transcranial magnetic stimulation (TMS) and cranial electrical stimulation. Medical coverage policy. http://apps.humana.com/tad/tad_new/Search.aspx?criteria=Tinnitus&searchtype=freetext&policyType=both. Published 2020. Accessed February 20, 2020.

202. Humana. Biofeedback. Medical coverage policy. http://apps.humana.com/tad/tad_new/Search.aspx?criteria=Tinnitus&searchtype=freetext&policyType=both. Published 2019. Accessed February 20, 2020.

203. Kaiser Permanente. Clinical review criteria. Tinnitus masking/retraining therapy. https://wa-provider.kaiserpermanente.org/static/pdf/hosting/clinical/criteria/pdf/tinret.pdf. Published 1998. Accessed February 9, 2020.

204. Regence Blue Shield Association. Transcranial magnetic stimulation as a treatment of depression and other disorders, Medicine, Policy No. 148. http://blue.regence.com/trgmedpol/medicine/med148.pdf. Published 2019. Accessed February 9, 2020.

205. System DHAotMH. TRICARE Policy Manual 6010.60-M, April 1, 2015. Chapter 8. Section 5.1 Medical devices. https://manuals.health.mil/pages/DisplayManualHtmlFile/TP15/38/AsOf/TP15/c8s5_1.html. Published 2015. Accessed February 20, 2020.

206. UnitedHealthcare. Transcranial magnetic stimulation (TMS). https://www.uhcprovider.com/content/provider/en/viewer.html?file=https%3A%2F%2Fwww.uhcprovider.com%2Fcontent%2Fdam%2Fprovider%2Fdocs%2Fpublic%2Fpolicies%2Fcomm-medical-drug%2Ftranscranial-magnetic-stimulation.pdf. Published 2019. Accessed February 20, 2020.

207. UnitedHealthcare. Durable Medical Equipment (DME), Prosthetics, Corrective Applicance/Orthotics (Non-Foot Orthotics) and Medical Supplies Grid. https://www.uhcprovider.com/content/provider/en/viewer.html?file=https%3A%2F%2Fwww.uhcprovider.com%2Fcontent%2Fdam%2Fprovider%2Fdocs%2Fpublic%2Fpolicies%2Fmedadv-coverage-sum%2Fdme-prosthetics-corrective-appliances-orthotics-med-supplies-grid.pdf. Published 2020. Accessed February 20, 2020.

208. Fuller TE, Haider HF, Kikidis D, et al. Different teams, same conclusions? A systematic review of existing clinical guidelines for the assessment and treatment of tinnitus in adults. *Frontiers in Psychology.* 2017;8.

Appendix A. State of Washington Health Care Authority Utilization Data

These data are pending from the State.

Appendix B. Additional Background

Table B1. FDA-Approved Tinnitus Sound-Masking Devices

Applicant	Product(s)	510k Number	Approval date
ADM Tronics Unlimited, Inc.	Aurex-3	K981704	8/5/1998
Amplisound Hearing Products & Services	Solace Sound Generators	K132965	3/25/2014
ANM Adaptive Neuromodulation GMBH	Tinnitus Therapy System ANM T30 Cr	K112752	12/16/2011
Associated Hearing Instruments	Micro Masker	K924991	6/14/1993
Audifon GMBH & Co. KG	Switch Trt	K091552	8/12/2009
Audifon-USA Inc.	Audifon Tinnitus Module	K171243	10/19/2017
	Audifon Arriva Cic, Is, Is+, M, S, S+, X Trt, Audifon Vico, Audifon Prado, Audifon Elia, Cic, Is, Is+, M, S Trt	K130514	11/21/2013
	Audifon Sueno Cic, Audifon Sueno S, Audifon Sueno T Cic, Audifon Sueno T S	K130417	9/12/2013
	Jump S+ Trt, Jump Cic Trt, Jump S Trt, Jump C Trt	K083488	2/19/2009
Audiotrone	T-570 Tinnitus Masker	K800701	4/10/1980
	TA-641 Tinnitus Instrument	K800702	5/8/1980
Beltone Electronics Corp.	Minuet Masker; Jubilee Masker	K800784	4/29/1980
Danavox Inc.	Behind-The-Ear Masking Amplifier, 735s	K780546	4/10/1978
General Hearing Instruments Inc.	Tranquil Tri-Bte	K061459	6/30/2006
	Tranquil Tri-Oe, Tranquil Tri-Coe, Tranquil Tri-Cic	K974751	3/6/1998
GN Hearing A/S	Tinnitus Sound Generator Module	K180495	11/30/2018
	Tinnitus Sound Generator Module	K181586	7/13/2018
GN Resound A/S	Tinnitus Sound Generator Module	K073636	3/13/2008
	Tinnitus Sound Generator Module	K110932	5/3/2011
	Tinnitus Sound Generator Module	K150171	5/14/2015
Hal-Hen Co. Inc.	Nuvox Bedside Tinnitus Masker	K802750	12/31/1980
Hansaton Akustik GMBH	Wave 2G Soul	K130937	1/3/2014
Hearing Innovations Inc.	Hisonic-Trd Tinnitus Relief Device	K013253	4/5/2002
Jiangsu Betterlife Medical Co. Ltd.	TinniLogic Mobile Tinnitus Management Device	K163094	5/17/2017
KW Ear Lab Inc.	Reve134	K151719	10/9/2015
LTMLT Inc.	Auditory Cassette	K941834	10/31/1994
Magnatone Hearing Aid Corp. DBA Persona Medical	Evok 900 Series Hearing Aid/Tinnitus Masker Option Device	K093715	12/22/2010
Marpac Inc.	Bedside Tinnitus Masker #1500	K802234	10/10/1980
	Model#1550 Marsona(R) Tinnitus Masker	K940567	7/6/1994
Melmedtronics, Inc.	The Inhibitor, Model 001	K070648	6/29/2007
Microbio-Medics Inc.	321Q Minimum Energy Tinnitus Suppressor	K922572	11/2/1992
Micro-Ear Technology Inc.	Refuge Sound Generator	K041302	7/1/2004
Neuromonics Pty Ltd.	Neuromonics Tinnitus Treatment	K043274	1/28/2005
Neurosim Limited	TST—Suppressor Model #1000	K013827	5/21/2002
Neurotherapies Reset GMBH	Desyncra for Tinnitus Therapy System Desyncra for Tinnitus Pro System	K151558	1/20/2016
Oticon A/S	Tinnitus Soundsupport	K133308	3/18/2014
Otoharmonics Corp	Levo Tinnitus Masking Software Device	K140845	7/18/2014
Petroff Audio Technologies	Digital Tinnitus Masking System	K974501	1/20/1998
Phonak LLC	Phonak Tinnitus Balance	K123450	2/11/2013

Applicant	Product(s)	510k Number	Approval date
Sanuthera Inc.	Serenity	K150014	7/27/2015
Siemens Hearing Instruments Inc.	TCI COMBI (Tinnitus Control Instrument Combination)	K003558	4/24/2001
	TCI (Tinnitus Control Instrument)	K003559	4/26/2001
	Custom TCI (Tinnitus Control Instrument)	K011364	6/7/2001
	Custom TCI COMBI (Tinnitus Control Instrument Combination)	K011366	6/1/2001
Sound Options Tinnitus Treatments Inc.	Sound Options Tinnitus Treatment	K161562	9/28/2016
Sound Technique System LLC	Ultraquiet	K021202	7/13/2002
SoundCure Inc.	SoundCure Serenade Tinnitus Treatment System	K150065	4/13/2015
	SoundCure Serenade Tinnitus Treatment System	K111293	8/24/2011
Spectral Visualization & Development Inc.	Quiescence	K040330	4/12/2004
Starkey Laboratories Inc.	Multiflex Tinnitus Technology	K122876	10/31/2012
	Crescent Tinnitus Retaining Sound Generator	K030180	9/17/2003
	Starkey TM-3 TM-5 High Frequency Tinnitus Masker	K964216	12/6/1996
	Starkey TM Air Conduction Tinnitus Masker	K963838	11/26/1996
	Starkey MA-3 Air Conduction Combination Hearing Aid/Tinnitus Masker	K963995	11/26/1996
	Model TM5 Behind Ear Tinnitus Masker	K791790	10/26/1979
	Hearing Aid Model MA-1	K791142	9/28/1979
	Model MA3 Behind-The-Ear Masker/Hearing	K791071	7/3/1979
	Tinnitus Masker	K781798	11/3/1978
Telex Communications Inc.	Telex Tinnitus-Companion	K984243	1/21/1999
Tinnitech Ltd.	ANMP (Acoustic Neuro Modulation Protocol)	K030791	4/17/2003
Tinnitus Control Inc.	Tinnitus Phase-Out	K061111	5/16/2006
	Tinnitus Rx	K031624	7/24/2003
Tinnitus Otosound Products LLC	Customized Sound Therapy (CST)	K070599	7/13/2007
Tinnitus Treatment Centers Inc.	TTCGHI-T and TTCTN3-T-T	K982451	5/7/1999
	Pillow Masker, C2007m, C2008m,Ce2000, Wonder Ear, Mini Wonder Ear, Pt-2sm, Pt-3sm, Pt-3lfm, Pt-3hfm, Pt3cm, Pt5-Sm, Pt5-	K982432	1/25/1999
Turtle Beach Corporation	Hypersound Tinnitus Module	K161331	8/23/2016
Unitron Hearing	Unitron Tinnitus Masker Feature	K130494	5/7/2013
Vican Instrument Co.	Tinnitus Maskers Model S584	K790190	2/12/1979
Vicon Instrument Co.	Tinnitus Maskers, Models S564&S574	K771769	1/3/1978
	Tinnitus Aid, Model S244	K770938	6/28/1977
Widex Hearing Aid Co. Inc.	Zen Program (Mind 440 Hearing Aid)	K080955	6/27/2008
Widex USA	IE-ZEN (In Clear Series Hearing Aid)	K110973	5/5/2011

Appendix C. Search Strategy

PubMed Search, Inception Through September 6, 2019

Search	Query	Items found
#1	Search ((“Tinnitus”[Mesh] OR tinnit*[tiab] OR (ear*[ti] AND (buzz*[ti] OR ring*[ti] OR roar*[ti] OR click*[ti] OR puls*[tiab])))	15954
#2	Search ((“Tinnitus”[Mesh] OR tinnit*[tiab] OR (ear*[ti] AND (buzz*[ti] OR ring*[ti] OR roar*[ti] OR click*[ti] OR puls*[tiab]))) Filters: English	13336
#3	Search ((“Tinnitus”[Mesh] OR tinnit*[tiab] OR (ear*[ti] AND (buzz*[ti] OR ring*[ti] OR roar*[ti] OR click*[ti] OR puls*[tiab]))) Filters: English; Adult: 19+ years	6920
#4	Search (“addresses”[pt] OR “autobiography”[pt] OR “bibliography”[pt] OR “biography”[pt] OR “case reports”[pt] OR “comment”[pt] OR “congresses”[pt] OR “dictionary”[pt] OR “directory”[pt] OR “festschrift”[pt] OR “government publications”[pt] OR “historical article”[pt] OR “interview”[pt] OR “lectures”[pt] OR “legal cases”[pt] OR “legislation”[pt] OR “news”[pt] OR “newspaper article”[pt] OR “patient education handout”[pt] OR “periodical index”[pt] OR "comment on" OR ("Animals"[Mesh] NOT "Humans"[Mesh]) OR rats[tw] OR cow[tw] OR cows[tw] OR chicken*[tw] OR horse[tw] OR horses[tw] OR mice[tw] OR mouse[tw] OR bovine[tw] OR sheep OR ovine OR murinae)	8988860
#5	Search (#3 NOT #4)	5041
#6	Search ("Cost-Benefit Analysis"[Mesh] OR "Counseling"[Mesh] OR "Disease Management"[Mesh] OR “Hearing Aids”[Mesh] OR "Perceptual Masking"[Mesh] OR "Psychotherapy"[Mesh] OR "Rehabilitation"[Mesh] OR "rehabilitation"[Subheading] OR "Rehabilitation Nursing"[Mesh] OR “therapeutic use”[subheading] OR "Therapeutics"[Mesh] OR "therapy"[Subheading])	9538735
#7	Search (#5 AND #6)	3190
#8	Search (CBT[tiab] OR cost-benefit[tiab] OR cost-effective*[tiab] OR cost*[tiab] OR costs[tiab] OR "disease management"[tiab] OR MBSR[tiab] OR MBTSR[tiab] OR mindfulness[tiab] OR rTMS[tiab] OR “sound generator”[tiab] OR “sound generators”[tiab] OR (sound[tiab] AND mask*[tiab]) OR “Tinnitus Retraining Therapy”[All Fields] OR TRT[tiab] OR “Neuromonics”[All Fields] OR NTT[tiab] OR “Progressive Tinnitus Management”[All Fields] OR PTM[tiab] OR TAT[tiab] OR therap*[tiab] OR TRT[tiab] OR “transcutaneous vagus nerve stimulation”[All Fields] OR treatment[tiab]) “Progressive Tinnitus Management”[All Fields] OR PTM[tiab] OR TAT[tiab] OR therap*[tiab] OR TRT[tiab] OR “transcutaneous vagus nerve stimulation”[All Fields] OR treatment[tiab])	6094234
#9	Search (#5 AND #8)	2048
#10	Search (#7 OR #9)	3462
#11	Search ((“Neuromonics Tinnitus Treatment”[All Fields] OR “Progressive Tinnitus Management”[All Fields] OR “Tinnitus Activities Treatment”[All Fields] OR “Tinnitus Retraining Therapy”[All Fields]))	167
#12	Search ((“Neuromonics Tinnitus Treatment”[All Fields] OR “Progressive Tinnitus Management”[All Fields] OR “Tinnitus Activities Treatment”[All Fields] OR “Tinnitus Retraining Therapy”[All Fields])) Filters: English	136
#13	Search ((“Neuromonics Tinnitus Treatment”[All Fields] OR “Progressive Tinnitus Management”[All Fields] OR “Tinnitus Activities Treatment”[All Fields] OR “Tinnitus Retraining Therapy”[All Fields])) Filters: English; Adult: 19+ years	56
#14	Search (#10 OR #13)	3462
#15	Search ((randomized[title/abstract] OR randomised[title/abstract]) AND controlled[title/abstract] AND trial[title/abstract]) OR (controlled[title/abstract] AND trial[title/abstract]) OR "controlled clinical trial"[publication type] OR "Randomized Controlled Trial"[Publication Type] OR "Single-Blind Method"[MeSH] OR "Double-Blind Method"[MeSH] OR "Random Allocation"[MeSH]	757389
#16	Search (#14 AND #15)	**649**

#17	Search (("Systematic Reviews as Topic"[Mesh] OR "systematic review"[ti] OR "meta-analysis"[pt] OR "meta-analysis"[ti] OR "systematic literature review"[ti] OR "this systematic review"[tw] OR ("systematic review"[tiab] AND review[pt]) OR meta synthesis [ti] OR "cochrane database syst rev"[ta]))	217343
#18	Search ((#14 AND #17) NOT #16)	**28**
#19	Search (("Cohort Studies"[Mesh] OR "Case-control Studies"[Mesh] OR "Comparative Study"[pt] OR "Risk Factors"[Mesh] OR "cohort"[tw] OR "compared"[tw] OR "groups"[tw] OR "case control"[tw] OR "multivariate"[tw]) OR (first[Title/Abstract] AND episode[Title/Abstract]) OR cohort[Title/Abstract]))	7580599
#20	Search ((#14 AND #19) NOT (#16 OR #18))	**1794**
#21	Search (#16 OR #18 OR #20) Saved in EndNote	**2471**

PubMed Yield: 2,471 (unchanged after deduplication)

Embase Search, Inception Through September 6, 2019

Search	Search History	Results
#1	'tinnitus'/exp OR 'tinnitus' OR tinnit*:ti,ab OR (ear*:ti,ab AND (buzz*:ti,ab OR ring*:ti,ab OR roar*:ti,ab OR click*:ti,ab OR puls*:ti,ab))	74,196
#2	('tinnitus'/exp OR 'tinnitus' OR tinnit*:ti,ab OR (ear*:ti,ab AND (buzz*:ti,ab OR ring*:ti,ab OR roar*:ti,ab OR click*:ti,ab OR puls*:ti,ab))) AND [humans]/lim AND [english]/lim	46,426
#3	#2 AND [adult]/lim	22,528
#4	#3 NOT ([animals]/lim NOT [humans]/lim OR rats OR cow OR cows OR chicken* OR horse OR horses OR mice OR mouse OR bovine OR sheep OR ovine OR murinae)	22,337
#5	#4 NOT ([conference abstract]/lim OR [conference review]/lim OR [data papers]/lim OR [editorial]/lim OR [letter]/lim OR [note]/lim OR [short survey]/lim)	18,461
#6	'biofeedback'/exp OR 'cost benefit analysis'/exp OR 'counseling'/exp OR 'disease management'/exp OR 'disease management program'/exp OR 'hearing aid'/exp OR 'masking'/exp OR 'psychotherapy'/exp OR 'rehabilitation'/exp OR 'therapy'/exp OR 'tinnitus retraining therapy'/exp OR 'treatment outcome'/exp	9,813,852
#7	#5 AND #6	8,840
#8	'biofeedback':ti,ab OR cbt:ti,ab OR 'cost-benefit':ti,ab OR 'cost effective*':ti,ab OR cost*:ti,ab OR costs:ti,ab OR 'disease management':ti,ab OR mbsr:ti,ab OR mbtsr:ti,ab OR mindfulness:ti,ab,kw OR neuromonics:ti,ab OR ntt:ti,ab OR ptm:ti,ab OR rehab*:ti,ab OR 'relaxation training':ti,ab OR (relax*:ti,ab AND therap*:ti,ab) OR rtms:ti,ab OR 'sound generator':ti,ab OR 'sound generators':ti,ab OR (sound:ti,ab AND mask*:ti,ab) OR tat:ti,ab OR therap*:ti,ab,kw OR 'transcutaneous vagus nerve stimulation':ti,ab OR treatment:ti,ab,kw OR 'trt':ti,ab OR treatment:ti,ab	8,483,949
#9	#5 AND #8	7,306
#10	'neuromonics tinnitus treatment':ti,ab OR 'progressive tinnitus management':ti,ab OR 'tinnitus activities treatment':ti,ab OR 'tinnitus retraining therapy':ti,ab	193
#11	#10 AND [humans]/lim AND [english]/lim AND [adult]/lim	80
#12	#11 NOT ([animals]/lim NOT [humans]/lim OR rats OR cow OR cows OR chicken* OR horse OR horses OR mice OR mouse OR bovine OR sheep OR ovine OR murinae)	80
#13	#12 NOT ([conference abstract]/lim OR [conference review]/lim OR [data papers]/lim OR [editorial]/lim OR [letter]/lim OR [note]/lim OR [short survey]/lim)	74
#14	#7 OR #9 OR #13	11,009
#15	'randomized controlled trial'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'random allocation'/exp OR 'controlled trial'/exp OR 'control trial' OR (('control':ab,ti OR 'controlled':ab,ti) AND 'trial':ab,ti)	7,217,032
#16	#14 AND #15	4,455
#17	#16 AND [medline]/lim	3,846
#18	#16 NOT #17	**609**

Search	Search History	Results
#19	'systematic review'/exp OR 'systematic review (topic)'/exp OR 'meta analysis'/exp OR 'meta analysis (topic)'/exp OR 'systematic literature review':ti,ab OR 'this systematic review':ti,ab OR 'umbrella review':ti,ab OR 'meta-analysis':ti,ab OR 'meta-analyses':ti,ab OR 'meta-synthesis':ti,ab OR 'meta-syntheses':ti,ab	396,550
#20	#14 AND #19	67
#21	#20 NOT #18	62
#22	#21 NOT [medline]/lim	**6**
#23	'case control study'/exp OR 'cohort analysis'/exp OR 'comparative study'/exp OR 'risk factor'/exp OR 'cohort' OR 'compared' OR 'multivariate' OR ('first':ti,ab AND ('episode':ti,ab OR 'cohort':ti,ab))	7,024,371
#24	#14 AND #23	3,734
#25	#24 NOT (#22 OR #18)	3,419
#26	#25 NOT [medline]/lim	**148**

Embase Yield: 746 (735 after deduplication)

Cochrane Library Search, Inception to September 6, 2019

ID	Search	Hits
#1	[mh Tinnitus] OR tinnit*:ti,ab OR (ear:ti AND (buzz*:ti,ab OR ring*:ti,ab OR roar*:ti,ab OR click*:ti,ab OR puls*:ti,ab))	1887
#2	[mh "Cost-Benefit Analysis"] OR [mh "Counseling"] OR [mh "Disease Management"] OR [mh "Hearing Aids"] OR [mh "Perceptual Masking"] OR [mh "Psychotherapy"] OR [mh "Rehabilitation"] OR [mh /RH] OR [mh "Rehabilitation Nursing"] OR [mh /TU] OR [mh /TH]	297606
#3	#1 AND #2	565
#4	CBT:ti,ab OR cost-benefit:ti,ab OR cost-effective*:ti,ab OR cost*:ti,ab OR costs:ti,ab OR "disease management":ti,ab OR MBSR:ti,ab OR MBTSR:ti,ab OR mindfulness:ti,ab OR rTMS:ti,ab OR "sound generator":ti,ab OR "sound generators":ti,ab OR (sound:ti,ab AND mask*:ti,ab) OR "Tinnitus Retraining Therapy":ti,ab,kw OR TRT:ti,ab OR "Neuromonics":ti,ab OR NTT:ti,ab OR "Progressive Tinnitus Management":ti,ab,kw OR PTM:ti,ab OR rehab*:ti,ab OR TAT:ti,ab OR therap*:ti,ab OR TRT:ti,ab OR "transcutaneous vagus nerve stimulation":ti,ab,kw OR treatment:ti,ab	792509
#5	#1 AND #4	1433
#6	#3 OR #5	1492
#7	"Neuromonics Tinnitus Treatment":ti,ab,kw OR "Progressive Tinnitus Management":ti,ab OR "Tinnitus Activities Treatment":ti,ab OR "Tinnitus Retraining Therapy":ti,ab	71
#8	#6 OR #7 in the Cochrane Library	1492
#9	#8 in Cochrane Database of Systematic Reviews	**34**

Cochrane Yield: 28 (24 after deduplication)

PsycINFO Search, Inception to September 9, 2019

#	Query	Limiters/Expanders	Last Run Via	Results
S1	DE "Tinnitus" OR TX tinnit* OR (TI ear* AND (TI buzz* OR TI ring* OR TI roar* OR TI click* OR TI puls*))	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	2,144

#	Query	Limiters/Expanders	Last Run Via	Results
S2	S1 NOT (PZ Abstract Collection OR PZ Bibliography OR PZ Chapter OR PZ Clarification OR PZ Column/Opinion OR PZ Comment/Reply OR PZ Dissertation OR PZ Editorial OR PZ Encyclopedia Entry OR PZ Letter OR PZ Obituary OR PZ Poetry OR PZ Publication Information OR PZ Reprint OR PZ Review-Book OR PZ Review-Media OR PZ Review-Software & Other OR MR INTERVIEW OR MR MATHEMATICAL MODEL OR MR SCIENTIFIC SIMULATION OR PT Encyclopedia OR PT Dissertation Abstract)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,672
S3	S2 NOT ((PO Animals NOT PO Humans) OR TX rats or TX cow or TX cows or TX chicken* or TX horse or TX horses or TX mice or TX mouse or TX bovine or sheep or ovine or murinae))	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,565
S4	S3	Limiters - English; Language: English; Age Groups: Adulthood (18 yrs & older), Young Adulthood (18-29 yrs), Thirties (30-39 yrs), Middle Age (40-64 yrs), Aged (65 yrs & older), Very Old (85 yrs & older) Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	932
S5	DE "Costs and Cost Analysis" OR DE "Budgets" OR DE "Cost Containment" OR DE "Health Care Costs" OR DE "Money"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	31,514
S6	S4 AND S5	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	2
S7	DE "Addiction Treatment" OR DE "Adjunctive Treatment" OR DE "Adventure Therapy" OR DE "Aftercare" OR DE "Anxiety Management" OR DE "Auditory Masking" OR DE "Behavior Modification" OR DE "Bibliotherapy" OR DE "Biofeedback" OR DE "Biofeedback Training" OR DE "Client Transfer" OR DE "Client Treatment Matching" OR DE "Cognitive Behavior Therapy" OR DE "Cognitive Techniques" OR DE	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	474,013

#	Query	Limiters/Expanders	Last Run Via	Results
	"Computer Assisted Therapy" OR DE "Counseling" OR DE "Creative Arts Therapy" OR DE "Cross Cultural Treatment" OR DE "Disease Management" OR DE "Habilitation" OR DE "Hospice" OR DE "Health Care Services" OR DE "Hearing Aids" OR DE "Human Potential Movement" OR DE "Human Services" OR DE "Hydrotherapy" OR DE "Institutionalization" OR DE "Integrated Services" OR DE "Interdisciplinary Treatment Approach" OR DE "Intervention" OR DE "Involuntary Treatment" OR DE "Language Therapy" OR DE "Life Sustaining Treatment" OR DE "Maintenance Therapy" OR DE "Masking" OR DE "Mental Health Programs" OR DE "Milieu Therapy" OR DE "Mind Body Therapy" OR DE "Mindfulness-Based Interventions" OR DE "Movement Therapy" OR DE "Multimodal Treatment Approach" OR DE "Multisystemic Therapy" OR DE "Neurotherapy" OR DE "Outpatient Treatment" OR DE "Pain Management" OR DE "Partial Hospitalization" OR DE "Personal Therapy" OR DE "Physical Treatment Methods" OR DE "Preventive Medicine" OR DE "Private Practice" OR DE "Psychoeducation" OR DE "Psychotherapy" OR DE "Rehabilitation" OR DE "Relaxation Therapy" OR DE "Respite Care" OR DE "Self-Help Techniques" OR DE "Social Casework" OR DE "Sociotherapy" OR DE "Speech Therapy" OR DE "Spiritual Care" OR DE "Symptoms Based Treatment" OR DE "Therapeutic Processes" OR DE "Treatment" OR DE "Treatment Barriers" OR DE "Treatment Compliance" OR DE "Treatment Dropouts" OR DE "Treatment Duration" OR DE "Treatment Effectiveness Evaluation" OR DE "Treatment Facilities" OR DE "Treatment Guidelines" OR DE "Treatment Outcomes" OR DE "Treatment Planning" OR DE "Treatment Process and Outcome Measures" OR DE "Treatment Refusal" OR DE "Treatment Termination" OR DE "Treatment Withholding" OR DE "Video-Based Interventions"			
S8	S4 AND S7	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases	203

#	Query	Limiters/Expanders	Last Run Via	Results
		Search modes - Boolean/Phrase	Search Screen - Advanced Search Database - PsycINFO	
S9	TX biofeedback* OR TX CBT OR TX cost-benefit OR TX cost-effective* OR TX cost* OR TX costs OR TX "disease management" OR TX hearing aid* OR TX MBSR OR TX MBTSR OR TX mindfulness OR TX rTMS OR TX "sound generator" OR TX "sound generators" OR (TX sound AND TX mask*) OR TX Neuromonics OR TX NTT OR TX PTM OR TX TAT OR TX therap* OR TX TRT OR TX "transcutaneous vagus nerve stimulation" OR TI treat* OR AB treat* OR TX treatment	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,325,565
S10	S4 AND S9	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	497
S11	TX "Neuromonics Tinnitus Treatment" OR TX "Progressive Tinnitus Management" OR TX "Tinnitus Activities Treatment" OR TX "Tinnitus Retraining Therapy"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	42
S12	S11 NOT (PZ Abstract Collection OR PZ Bibliography OR PZ Chapter OR PZ Clarification OR PZ Column/Opinion OR PZ Comment/Reply OR PZ Dissertation OR PZ Editorial OR PZ Encyclopedia Entry OR PZ Letter OR PZ Obituary OR PZ Poetry OR PZ Publication Information OR PZ Reprint OR PZ Review-Book OR PZ Review-Media OR PZ Review-Software & Other OR MR INTERVIEW OR MR MATHEMATICAL MODEL OR MR SCIENTIFIC SIMULATION OR PT Encyclopedia OR PT Dissertation Abstract)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	28
S13	S12 NOT ((PO Animals NOT PO Humans) OR TX rats or TX cow or TX cows or TX chicken* or TX horse or TX horses or TX mice or TX mouse or TX bovine or sheep or ovine or murinae))	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	27
S14	S13	Limiters - English; Language: English; Age Groups: Adulthood (18 yrs & older), Young Adulthood (18-29 yrs), Thirties (30-39 yrs), Middle Age (40-64 yrs), Aged (65 yrs & older)	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	13

#	Query	Limiters/Expanders	Last Run Via	Results
		Expanders - Apply equivalent subjects Search modes - Boolean/Phrase		
S15	S6 OR S8 OR S10 OR S14	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	510
S16	DE "Randomized Clinical Trials" OR DE "Randomized Controlled Trials" DE "Randomized Clinical Trials" OR DE "Randomized Controlled Trials" OR DE "Experiment Controls" OR (TX control* AND TX trial*)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	88,327
S17	S15 AND S16	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	**70**
S18	MR Systematic Review OR MR META ANALYSIS OR MR METASYNTHESIS OR TI “systematic review” OR AB “systematic review” OR TI “meta-analysis” OR TI “meta analysis” OR TI “systematic literature review” OR TX “this systematic review” OR TI “meta synthesis” OR TI “metasynthesis”	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	47,552
S19	S15 AND S18	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	**4**
S20	DE "Cohort Analysis" OR TX cohort* OR TX "case control" OR TX "case-control" OR TX "case controlled" OR TX "case-controlled" OR TX multivariate OR #TX first and TX episode#	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	178,170
S21	S15 AND S20	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	**35**

PsycINFO Yield: 59 (23 after deduplication)

Total Bibliographic Database Yield: 3,304 (3,253 after deduplication)

ClinicalTrials.Gov Search

On August 6, 2019, a search for "Tinnitus" clinicaltrials.gov yielded 225 interventions, 139 of which were non-pharmacologic interventions within the scope of this HTA. Of these studies, 78 were completed, 18 of which reported having results.

Other Data

We searched websites of the organizations listed in Table B-1 to identify related health technology assessment, clinical practice guidelines, position or policy statements, payor coverage policies, or other clinical guidance.

Table B1. Websites Searched for Documents Relevant to Treatment of Tinnitus

Organization	Potentially Relevant Documents
American Speech-Language-Hearing Association	5
American Academy of Audiology	0
Institute of Medicine	0
American Tinnitus Association	0
American Auditory Society	0
American Otologic Society	0
American Academy of Otolaryngology – Head and Neck Surgery	0
U.S. Department of Veteran's Affairs – National Center for Rehabilitative Auditory Research	0
American Family Physician	0
British Academy of Audiology	1
ECRI Institute	0
Turning Research Into Practice (TRIP) Database	0
National Institute for Clinical Excellence	3
Institute for Clinical and Economic Review	0
University of York Centre for Reviews and Dissemination/National Institutes for Health Research	6
U.S. Food and Drug Administration	0
U.S. Agency for Healthcare Research and Quality	1
Centers for Medicare and Medicaid Services	1
Veterans Affairs Evidence Synthesis Program	0
Aetna	1
Cigna	2
Humana	2
BlueCross BlueShield (Premera and Regence)	2
Kaiser Permanente	1
United Health	1
TRICARE	1

Abbreviations: U.S. = United States

Appendix D. Evidence Tables

Table D1a. Study Characteristics for Included Sound Therapy Interventions D-2
Table D1b. Population Characteristics for Included Sound Therapy Interventions D-3
Table D1c. Intervention Characteristics for Included Sound Therapy Interventions D-7
Table D1d. Efficacy Outcomes for Sound Therapy Interventions D-11
Table D1e. Safety and Cost Outcomes for Sound Therapy Interventions D-19
Table D2a. Study Characteristics for Included Repetitive Transcranial Magnetic Stimulation Interventions D-21
Table D2b. Population Characteristics For Included Repetitive Transcranial Magnetic Stimulation Interventions D-23
Table D2c. Intervention Characteristics for Included Repetitive Transcranial Magnetic Stimulation Interventions D-29
Table D2d. Efficacy Outcomes for Included Repetitive Transcranial Magnetic Stimulation Interventions D-35
Table D2e. Safety and Cost Outcomes for Included Repetitive Transcranial Magnetic Stimulation Interventions D-48
Table D3a. Study Characteristics For Included Cognitive Behavioral Interventions D-51
Table D3b. Population Characteristics for Included Cognitive Behavioral Therapy Interventions D-53
Table D3c. Intervention Characteristics for Included Cognitive Behavioral Therapy Interventions D-60
Table D3d. Efficacy Outcomes for Included Cognitive Behavioral Therapy Interventions D-66
Table D3e. Safety and Cost Outcomes for Included Cognitive Behavioral Therapy Interventions D-82
Table D4a. Study Characteristics for Included Tinnitus-Specific Interventions D-84
Table D4b. Populations Characteristics of Included Tinnitus-specific Interventions D-85
Table D4c. Intervention Characteristics of Included Tinnitus-specific Interventions D-89
Table D4d. Efficacy Outcomes for Included Tinnitus-specific Interventions D-93
Table D4e. Safety and Cost Outcomes for Included Tinnitus-specific Interventions D-101

Table D1a. Study Characteristics for Included Sound Therapy Interventions

Authors (Year)	Study Design	Sponsor	Country	Eligible Study Arms	Total N Overall/ Total N in Eligible Study Arms	Risk of Bias
Davis et al. (2008)[24]	RCT	Neuromonics Pty. Ltd.	Australia	Counseling only Neuromonics	69/ 69	High
Dineen et al. (1999)[19] Dineen et al. (1997)[190] Dineen et al. (1997)[25]	RCT	NR, although Starkey Laboratories donated custom TM devices for the study	Australia	Information only Information with sound device	96/ 48	High
Henry et al. (2017)[16]	RCT	Phonak LLC, Department of Veterans Affairs RR&D Service	U.S.	Hearing aid Hearing aids with sound generator	55/ 37	Some concerns
Henry et al. (2015)[189]	RCT	Starkey Hearing Technologies and Department of Veteran's Affairs RR&D	U.S.	Hearing aid control Hearing aid + sound generator	30/ 30	Some concerns
Hiller et al. (2005)[23]	RCT	The German Tinnitus Association, Interton GmbH, and Audioplast GmbH	Germany	Tinnitus education or CBT Tinnitus education or CBT plus sound generator	136/ 136	Some concerns
Li et al. (2016)[17]	RCT	Ontario Brain Institute	Canada	Control music Altered music	50/ 50	High
Okamoto et al. (2010)[22]	RCT	Deutsche Forschungsgemeinschaft and the Tinnitus Research Initiative.	Germany	Placebo music Monitoring	39/ 39	High
Schad et al. (2018)[15]	RCT	National Center for Rehabilitative Auditory Research	U.S.	Placebo Notched noise	30/ 30	High
Stein et al. (2016)[20]	RCT	Interdisciplinary Center for Clinical Research, University of Munster (Germany)	Germany	Placebo Tailor-made notched music training	100/ 100	Some concerns
Strauss et al. (2015)[21]	RCT	NR	Germany	Hearing aid control Hearing aid + notched environmental sound technology	20/ 20	Some concerns
Wise et al. (2016)[18]	RCT	Tinnitus Research Initiative	New Zealand	Control game Terrain game	50/ 50	High

Abbreviations: CBT = cognitive behavioral therapy; NR = not reported; RCT = randomized controlled trial; RR&D = rehabilitation, research and development; U.S. = United States.

Table D1b. Population Characteristics for Included Sound Therapy Interventions

Authors (Year)	Study Population	Mean Age (SD)	N (% Female)	N (%) Race/Ethnicity	Other Characteristics
Davis et al. (2008)[24]	Adults with bothersome tinnitus *Inclusion:* Tinnitus-related disturbance (> 17 on TRQ), ENT evaluation confirmed medical treatment for tinnitus was not feasible *Exclusion:* Significant hearing loss, clinically significant mental health condition, continued exposure to conditions that could aggravate tinnitus, concurrent treatment including recent onset of hearing aid use or treatment that exceeded 1 hour per day, ongoing monetary compensation claims related to tinnitus.	49.8 (15.8)	24 (48.0*)	NR	*Tinnitus Duration* Mean (SD) in years: 3.6 (4.1) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled.
Dineen et al. (1999)[19] Dineen (1997)[190] Dineen (1997)[25]	Adults recruited via community announcements that were disseminated by a speech and hearing clinic. *Inclusion:* NR *Exclusion:* NR	53.6 (15.0)# Range: 21 to 87#	28# (58.3*)	NR	*Tinnitus Duration* Length of time since becoming aware of tinnitus (y): Mean (median): 11.9 (6)# Range: 1 to 53# *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled *Other* Noise exposure (not explicitly defined): 32 (33.3*)#
Henry et al. (2017)[16]	Adults with suspected hearing loss and bothersome tinnitus were recruited from the community, local VA, and a tinnitus research center. *Inclusion:* TFI score ≥20 (changed from 25 to 20 partway into study); THS score of ≥4; MoCA score ≥26 (max. 30); must have hearing loss within the aidable range. *Exclusion:* Use of hearing aids within 6 months; could not be fitted bilaterally with both types of hearing aids in the study.	HA: 61 (Range 48 to 75) HA+SG: 64 (Range 54 to 75)	HA: 4 (22) HA+SG: 4 (21)	NR	*Tinnitus Duration* NR *Hearing Loss* Hearing loss was an explicit inclusion criterion
Henry et al. (2015)[189]	Adults with bothersome tinnitus who were hearing aid candidates who were recruited	67.2 (9.2)	10* (33)	Caucasian: 27* (90)	*Tinnitus Duration* N (%) yrs tinnitus duration

Authors (Year)	Study Population	Mean Age (SD)	N (% Female)	N (%) Race/Ethnicity	Other Characteristics
	from previous research participation at the NCRAR or via newspaper advertisements. *Inclusion:* Adults (≥18 yrs) with clinically significant tinnitus (TFI score ≥25) and perceived hearing difficulties (candidate for hearing aid), no hearing aid experience within the last year, and had no mental, emotional, or health conditions that would prevent participation. *Exclusion:* Active external ear disease or conductive component to hearing loss; diagnosis of retro-cochlear pathology, Meniere's, endolymphatic hydrops, or perilymphatic fistula; presence of medical contraindications to a hearing aid fitting (including sudden-onset hearing loss, ear pain, vertigo, etc.).			Non-Caucasian 3* (10)	<1: 1* (3) 1-2: 2* (7) 3-5: 1* (3) 6-10: 3* (10) 11-20: 8* (27) >20: 12* (40) Unsure: 3* (10) *Hearing Loss* Hearing loss was an explicit inclusion criterion *Other* N (%) veterans: 13* (43) N (%) veterans receiving service-connected disability award for hearing loss or tinnitus: 2/13* (15)
Hiller et al. (2005)[23]	Adults outpatients with tinnitus duration >6 mos, recruited by newspaper adds or referral from their ENT. *Inclusion:* Patients with chronic (>6-mo duration) tinnitus causing psychological concerns or distress, with no current indication for standard medical treatment, and no current mental disorders that might require intense individual psychotherapy. All patients were additionally required to be motivated to participate in a psychological treatment approach. *Exclusion:* NR	Education: 45.2 (14.1) Education + Sound: 52.5 (15.3) CBT: 51.4 (10.9) CBT + Sound: 51.0 (13.2)	Education: 13* (39) Education + Sound: 15* (48) CBT: 17*(59) CBT + Sound: 10* (32)	NR	*Tinnitus Duration* N (%) with tinnitus duration >5 yrs Education: 4* (12) Education + Sound: 11* (36) CBT: 9* (31) CBT + Sound: 11* (36) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled *Other* N (%) with acoustic trauma Education: 1* (3) Education + Sound: 2* (7) CBT: 0* (0) CBT + Sound: 4* (13) N (%) with long-standing exposure to noise Education: 2* (6) Education + Sound: 5* (16) CBT: 3* (10) CBT + Sound: 5* (16)

Authors (Year)	Study Population	Mean Age (SD)	N (% Female)	N (%) Race/Ethnicity	Other Characteristics
Li et al. (2016)[17]	Adults with tinnitus recruited via advertisements and audiology clinics. *Inclusion:* Adults (≥18 yrs) with tinnitus for ≥1 yr; ability to listen to ≥2 hrs/d of music for 1 yr; able to speak and read English. *Exclusion:* THI score <26; absolute hearing thresholds >70 dB HL for corresponding frequencies <8 kHz; history of neurological/psychiatric disorders; severe hyperacusis or Ménière's disease; expectation to take ototoxic medication or experience constant loud noise exposure during study.	Control music: 55.8 (8.5) Altered music: 55.2 (13.9)	Control music: 10* (40)* Altered music: 6* (24)*	NR	*Tinnitus Duration* N (%) with tinnitus symptoms present for ≥10 yrs. Control music: 12 (48) Altered music: 9 (36) *Hearing Loss* Persons with hearing loss were explicitly excluded
Okamoto et al. (2010)[22]	Patients suffering from chronic, tonal tinnitus for > = 12 mos. *Inclusion:* Chronic (≥12 mos), unilateral/strongly lateralized, tonal tinnitus with a frequency ≤8 kHz. *Exclusion:* Significant hearing impairment, neurological or psychiatric complications.	40.5 (10.8)	NR	NR	*Tinnitus Duration* Mean (SD) duration in years 5.3 (5.6) *Hearing Loss* Persons with significant hearing impairment were excluded.
Schad et al. (2018)[15]	Adults with constant, bothersome tinnitus were recruited from a tinnitus research center. *Inclusion:* TFI score ≥20; not a candidate for hearing aids; no single-frequency air-bone gap >15 dB; and tinnitus frequency 3000 to 10,000 Hz. *Exclusion:* No diagnosis of significant hearing loss	58 (range 27-71)	Approximately 10 (1/3rd of study population)	NR	*Tinnitus Duration* NR *Hearing Loss* Persons with hearing loss were explicitly excluded
Stein et al. (2016)[20]	Adults with chronic, tonal tinnitus, recruited via newspaper and website advertisements and distribution of flyers to local ENT physicians. *Inclusion:* Adults (18 to 70 yrs) with chronic (≥3 months), tonal tinnitus with dominant frequencies 1 to 12 kHz *Exclusion:* Hearing loss above 70 dB HL in	47.5 (10.8)	33* (33)	NR	*Tinnitus Duration* Mean (SD) years since tinnitus onset: Placebo: 9.0 (6.8) Music training: 7.0 (7.3) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled

Authors (Year)	Study Population	Mean Age (SD)	N (% Female)	N (%) Race/Ethnicity	Other Characteristics
	the frequency ranges of one half octave above/below the tinnitus frequency, bilateral tinnitus with dominant frequency differing between the ears. Severe chronic or acute otological, mental or neurological disorders/diseases; consumption of illegal drugs or alcohol above WHO recommended limit; other current tinnitus or other therapies that might interfere with the trial, and participation in another clinical trial.				
Strauss et al. (2015)[21]	Patients with tonal tinnitus , recruited from a hearing rehabilitation and tinnitus center. *Inclusion:* Adults with tonal tinnitus. *Exclusion:* NR	Control: 53.5 (4.8) Sound: 52.7 (5.85)	Control: 1 (10*) Sound: 2 (20*)	NR	*Tinnitus Duration* NR *Hearing Loss* Hearing loss was not required or excluded, and no mention of this characteristic was made in describing the study population
Wise et al. (2016)[18]	Adults with chronic tinnitus that was identified as at least mildly problematic, recruited via university research database *Inclusion:* Adults (18 to 70 years) with moderate nonconductive hearing loss (<80 dB HL, 2 to 8 kHz) who reported having tinnitus for ≥ 6 mos, and indicated tinnitus was at least a mild problem (tinnitus rating scale). Required to be willing to play a computer game for 30 minutes/day for 20 consecutive days. *Exclusion:* NR	Control game: 62.3 (4.6)# Terrain:, 52.3 (10.6)#	10 (32.3*)#	NR	*Tinnitus Duration* Mean (SD) years tinnitus duration# Tetris: 16.0 (12.7) Terrain: 5.7 (8.6) *Hearing Loss* Hearing loss was an explicit inclusion criterion

Notes: * Indicates a data value that we calculated based on data provided in the publication.# Indicates that the data was only reported for study completers, not the number that was randomized.

Abbreviations: CBT = cognitive behavioral therapy; dB (HL) = decibels (in hearing level); ENT = ear nose and throat; HA = hearing aid; (k)Hz = (kilo)hertz; MoCA = Montreal cognitive assessment; mos = months; N = number; NA = not applicable; NCRAR = national center for rehabilitative auditory research; NR = not reported; SD = standard deviation; SG = sound generator; TFI = tinnitus functional index; THI = tinnitus handicap index; THS = tinnitus and hearing survey; TRQ = tinnitus reaction questionnaire; WHO = world health organization; yr = year.

Table D1c. Intervention Characteristics for Included Sound Therapy Interventions

Authors (Year)	Duration of Intervention	Control Group (N randomized or enrolled)	Intervention Group(s) (N randomized or enrolled)	Fidelity
Davis et al. (2008)[24]	12 mos	Counseling Only (13) Individual counseling based on principles of CBT that explained cause of tinnitus and coping strategies (e.g., avoid silence, overprotection, and loud noises). Received additional counseling time to equal amount of time with clinicians as intervention groups.	Neuromonics (22) Fitted with acoustic stimulus device in the form of music, instructed to listen for at least 2 hours per day, when tinnitus was most disturbing. 13 of 22 patients instructed to set device at level that just covered up tinnitus and 9 of 22 instructed to set volume to cover tinnitus for only half of the time spent wearing the device. Taught relaxation strategies facilitated by acoustic stimulus. Individual counseling based on principles of CBT that explained cause of tinnitus and coping strategies (e.g., avoid silence, overprotection, and loud noises). Sound + counseling (15) Fitted with acoustic stimulus device that emulated output of broadband noise generator, instructed to listen for as long as possible and a minimum of 2 hours per day, when tinnitus was most disturbing, with volume set to the lowest level at which both acoustic stimulus and tinnitus could be heard. Individual counseling based on principles of CBT that explained cause of tinnitus and coping strategies (e.g., avoid silence, over protection, and loud noises).	Mean (SD) hours of use per day Neuromonics: 1.8 (1.4) Sound + Counseling: 1.4 (1.1)
Dineen et al. (1999)[19] Dineen (1997)[190] Dineen (1997)[25]	NR	Information only (28) Received information (two 3-hour sessions) and written 60-page manual about tinnitus (e.g., prevalence, function of the auditory system), which included some mention of treatment strategies.	Information with sound device (20) Received informational materials and long-term, broad band noise provided via custom Starkey TM devices that provided stable wide-band noise across a wide frequency range.	NR
Henry et al. (2017)[16]	About 4 to 5 mos.	Hearing aid (HA) (18) RIC hearing aid (Audeo Q90 312-T; Phonak)	Hearing aids with sound generator (HA+SG) (19) RIC hearing aid (Audeo Q90 312-T; Phonak) that incorporated sound generation. The adjustable sound options included broadband noise, pink noise, and spectrally shaped sound based on user's hearing loss.	NR
Henry et al. (2015)[189]	3-4 mos	Hearing Aid Control (15) Commercially available RIC hearing aids with sound-generating capabilities, which were fitted binaurally, and adjusted for	Hearing Aid + Sound Generator (15) Commercially available RIC hearing aids with sound-generating capabilities, which were fitted binaurally, and adjusted for each individual. Identical, scripted tinnitus	Mean number of hours of use per day at final visit Control: 6.9 (right and left) Sound: 7.0 (right); 6.9 (left)

Authors (Year)	Duration of Intervention	Control Group (N randomized or enrolled)	Intervention Group(s) (N randomized or enrolled)	Fidelity
		each individual. The sound-generating feature was not turned on. Identical, scripted tinnitus counselling sessions occurred for both groups immediately after the HA fitting. All devices had data-logging capabilities to capture hrs/d of use.	counselling sessions occurred for both groups immediately after the HA fitting. The sound-generating feature was activated and adjustment once counseling ended. Participants could select slow, medium, or fast modulation rates, or no modulation. All devices had data-logging capabilities to capture hrs/d of use.	
Hiller et al. (2005)[23]	Education arm: Four 90-minute weekly sessions CBT arm: Ten 120-minute weekly sessions	Tinnitus education or CBT (69) Participants with mild tinnitus (TQ < 40) were provided with education which consisted of four 90-minute sessions about the physiology and anatomy of the hearing process, the nature of tinnitus, etiological mechanisms and treatment options. Patients were advised to avoid silence in their everyday environments, and were given materials about tinnitus, and encouraged to ask questions. Participants with moderate to severe tinnitus (TQ >40) were provided with CBT which consisted of ten 120-minute sessions that adapted the classical components of CBT for tinnitus treatment. Both types of treatment were provided in groups of 8 to 10 participants.	Tinnitus Education or CBT Plus Sound Generator (67) In addition to the tinnitus education or CBT, the treatment group received behind-the-ear broadband noise generators (one per-ear). Participants were instructed on how to use the devices, and told to wear them as often as possible, especially in quiet surroundings, and for at least 6 hrs/day.	Education: 29 of 31 were still wearing sound generator for at least 1 hour per day at the immediate post-treatment followup and 23 continued to wear at 6 mos. followup. CBT: 24 of 31 were still wearing sound generator for at least 1 hour per day at the immediate post-treatment followup and 13 continued to wear at 6 mos. followup
Li et al. (2016)[17]	1 yr	Control music (25) Unaltered 6-hr package of classical music, MP3 players, and choice of headphones or earbuds. Participants were instructed to listen for 2 hrs/day; those with hearing aids were directed to remove hearing aids while listening.	Altered music (25) Altered 6-hr package of classical music, altered using software (Sound Options Tinnitus Treatments Inc.) to create spectral content within music and customized based on the individual's hearing and tinnitus characteristics. Patients also received MP3 players and choice of headphones or earbuds. Participants were instructed to listen for 2 hrs/day; those with hearing aids were directed to remove hearing aids while listening.	NR

Authors (Year)	Duration of Intervention	Control Group (N randomized or enrolled)	Intervention Group(s) (N randomized or enrolled)	Fidelity
Okamoto et al. (2010)[22]	1 yr	Placebo music (13) Patients provided their favorite music, which was copied and filtered individually according to the placebo (moving) notched protocol. For the placebo group, a moving filter of one octave width, sparing the tinnitus frequency region, was supplied, and jumped incrementally up or down in a random fashion after 5 seconds of filtering. Frequency bands below 707 Hz and 15,321 Hz were not filtered. Participants were instructed to listen to the music daily, but no specific duration of listening was reported.	Monitoring (13) The monitoring group received no treatment. The monitoring group was not actually randomized; it consisted of eligible subjects who did not have time to listen to music and thus failed the run-in phase. Notched music (13) Patients provided their favorite music, which was copied and filtered individually according to the target (fixed) notched protocol, in which the frequency band of one octave width centered at the individual tinnitus frequency was removed from the music energy spectrum. Frequency bands below 707 Hz and 15,321 Hz were not filtered. Participants were instructed to listen to the music daily, but no specific duration of listening was reported.	Mean (SD) listening time per week: 12.4 hours (3.5)
Schad et al. (2018)[15]	2 wks	Placebo (10) Low-frequency noise (250-700 Hz) well below any participants' tinnitus frequencies administered via iPod Nano with Ety-Kids 5 earphones; instructed to wear 6 (awake) hours per day	Notched noise (10) 1000 to 12,000 Hz notched frequency noise within a 1-octave range centered around the tinnitus pitch match frequency; administered via iPod Nano with Ety-Kids 5 earphones; instructed to wear 6 (awake) hours per day Matched noise (10) Noise within a 1-octave wide band centered around the tinnitus pitch match frequency; administered via iPod Nano with Ety-Kids 5 earphones; instructed to wear 6 (awake) hours per day	Patients self-reported compliance (listening for 6+ hrs/day over 14 days). Only 5 patients reported perfect compliance (4 in placebo, 1 in notched). Mean (SD) hrs/day listening Placebo: 5.5 (1.7) Notched: 5.8 (1.0) Matched: 5 (1.9) Percent of time participants met compliance Placebo: 83 Notched: 85 Matched: 71
Stein et al. (2016)[20]	3 mos	Placebo (50) Patients provided 10 CDs of their favorite music, which was imported into the music library of a mobile device that they were given, which was installed with an iOS application to modify the music as needed. They also received closed headphones (Sennheiser HD 201). A moving notch filter with the same bandwidth as the treatment condition was	Tailor-made notched music training (50) Patients provided 10 CDs of their favorite music, which was imported into the music library of a mobile device that they were given, which was installed with an iOS application to modify the music as needed. They also received closed headphones (Sennheiser HD 201). The frequency band centered at the individual tinnitus frequency of each participant was removed from the music energy spectrum with three procedures that aimed to increase the lateral inhibition effect within the notch area	Participants listened to music on a mean of 71.6 (SD 16.3) days for an average of 115.3 (SD16.0) minutes per day. No difference in adherence between groups.

Authors (Year)	Duration of Intervention	Control Group (N randomized or enrolled)	Intervention Group(s) (N randomized or enrolled)	Fidelity
		applied, and the filter selected frequency bands at random. Participants instructed to listen to music for at least 2 hours per day for 12 weeks.	corresponding to the tinnitus frequency. Participants instructed to listen to music for at least 2 hours per day for 12 weeks.	
Strauss et al. (2015)[21]	3 wks	Hearing aid control (10) Provided with commercially available digital behind-the-ear hearing aid and instructed to keep a listening diary.	Hearing aid + notched environmental sound technology (10) Received the same commercially available hearing aid as the control group but implemented using an individually adjusted digital superimposed bi-quad notch filter, centered around the pure tone tinnitus frequency. Patients were instructed to keep a listening diary.	NR
Wise et al. (2016)[18]	20 days	Control game (16) The control group played a custom version of Tetris (without sound effects, 5 levels of increasing difficulty). All patients were given earphones (Apple iPod) and each day's game started with tinnitus assessment screens to calibrate the game. All participants were given verbal instructions about loading and playing the study game.	Terrain game (15) The treatment group game ("Terrain") was programmed to begin with a tinnitus assessment identical to the one presented in the control game. The game required that patients move through a virtual auditory landscape towards a pulsing target sound (dissimilar to their tinnitus) while ignoring "distracter" sounds (sometimes matched to the individual's tinnitus), utilizing their keyboard arrow keys to navigate. Movement towards the target sound increased intensity, and once the patient identified it they were awarded a point, and play resumed. The game included 5 levels, each of which offered new and additional distracter sounds. Study games were developed using software (LabVIEW, v.8) and all participant's home computers needed to have the appropriate operating system (Windows XP or 7). All patients were given earphones (Apple iPod) and verbal instructions about loading and playing the study game.	NR

Abbreviations: CBT = cognitive behavioral therapy; CD = compact disc; hrs = hours; Hz = hertz; mos = months; N = number; RIC = receiver-in-canal; SD = standard deviation; TQ = tinnitus questionnaire; yr = year.

Table D1d. Efficacy Outcomes for Sound Therapy Interventions

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Not sure)	Results
Davis et al. (2008)[24] Counseling only (13) Neuromonics (22) Sound + counseling (15)	Tinnitus Reaction Questionnaire Yes	Repeated measures over 6 months followup Neuromonics had lower mean score compared to control according to figures in publication, but actual values and statistical significance testing NR Sound + counseling had similar scores compared with control; *P* NS Repeated measures over 12 months followup Neuromonics had significantly lower scores compared to control; actual values NR; *P* = 0.014 Sound + counseling had similar scores compared with control; *P* = 0.606 % with score < 17 at 6 months Control: 31 Neuromonics: 64; *P* = 0.07 vs. control (RD* 33.3% (95% CI, 1.2% to 65.43%; RR* 2.1 [95% CI, 0.87 to 5.0]) Sound + counseling: 33; *P* = 0.91 vs. control (RD*2.3% [95% CI, -32.2% to 36.9%]; RR 1.1 [95% CI, 0.36 to 3.2])
	VAS for tinnitus loudness No	Repeated measures over 12 months Neuromonics had significantly lower scores compared with control; *P* < .001 Sound + counseling had similar scores compared with control; *P* = 0.091
	VAS-tinnitus severity No	Repeated measures over 12 months Neuromonics had significantly lower scores compared with control; *P* < 0.001 Sound+ counseling had similar scores compared with control; *P* = 0.884
	VAS-General relaxation level No	Repeated measures over 12 months Neuromonics had significantly lower scores compared to control; *P* = 0.003 Sound + counseling had similar scores compared with control; *P* = 0.696
Dineen et al,.(1999)[19] Dineen et al. (1997)[190] Dineen et al. (1997)[25] Information only (28) Information with sound device (20)	Tinnitus Reaction Questionnaire Not sure	Mean Score (SD), N Baseline Information: 29.2 (23.8), 28 Information + sound: 30.3 (27.4), 20 3 mo. Information: 19.9 (17.6), 18 Information + sound: 25.8 (25.0), 13 Calculated between-group difference (unadjusted for baseline) 5.9 (95% CI, -9.7 to 21.5); *P* = 0.45 Calculated between-group difference (adjusted for baseline): 4.8 (*P* value not calculable) 12 mo. Information: 19.4 (16.5), 17 Information + sound: 20.5 (17.7), 12 Calculated between-group difference (unadjusted for baseline): 1.1 (95% CI, -12.1 to 14.3); *P* = 0.87 Calculated between-group difference (adjusted for baseline): 0.0 (*P* value not calculable)
	VAS for tinnitus	Mean score (SD), N

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Not sure)	Results
	loudness No	Baseline Information: 6.2 (2.1), 28 Information + sound: 6.3 (3.1), 20 3 mo. Information: 5.5 (2.3), 18 Information + sound: 5.6 (2.4), 13 Calculated between-group difference (unadjusted for baseline): 0.1 (95% CI, -1.6 to 1.8); *P* = 0.91 Calculated between-group difference (adjusted for baseline): 0.0 (*P* value not calculable) 12 mo. Information: 5.8 (1.9), 17 Information + sound: 5.3 (2.2), 12 Calculated between-group difference (unadjusted for baseline): -0.5 (95% CI, -2.1 to 1.1); *P* = 0.52 Calculated between-group difference (adjusted for baseline): -0.6 (*P* value not calculable)
	VAS for tinnitus annoyance No	Mean score (SD), N Baseline Information: 6.0 (2.4), 28 Information + sound: 6.2 (3.2), 20 3 mo. Information: 4.4 (2.3), 18 Information + sound: 4.2 (2.9), 13 Calculated between-group difference (unadjusted for baseline): -0.2 (95% CI, -2.1 to 1.7); *P* = 0.83 Calculated between-group difference (adjusted for baseline): -0.4 (*P* value not calculable) 12 mo. Information: 4.3 (2.3), 17 Information + sound: 3.7 (2.6), 12 Calculated between-group difference (unadjusted for baseline): -0.6 (95% CI, -2.5 to 1.3); *P* = 0.52 Calculated between-group difference (adjusted for baseline): -0.8 (*P* value not calculable)
	VAS for tinnitus coping No	Mean Score (SD), N Baseline Information: 7.5 (2.0), 28 Information + sound: 6.9 (3.4), 20 3 mo. Information: 8.0 (1.5), 18 Information + sound: 7.1 (2.1), 13 Calculated between-group difference (unadjusted for baseline): -0.9 (95% CI, -2.2 to 0.4); *P* = 0.17 Calculated between-group difference (adjusted for baseline): -0.3 (*P* value not calculable) 12 mo.

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Not sure)	Results
		Information: 4.3 (2.3), 17 Information + sound: 3.7 (2.6), 12 Calculated between-group difference (unadjusted for baseline): -0.6 (95% CI, -2.5 to 1.3); *P* = 0.52 Calculated between-group difference (adjusted for baseline): 0.0 (*P* value not calculable)
	Ways of Coping Check List Revised No	Emotion-focused coping subscale, mean score (SD), N Baseline Information: 17.3 (13.7), 28 Information + sound: 13.0 (10.0), 20 12 mo. Information: 16.8 (10.1), 17 Information + sound: 15.2 (11.2), 12 Calculated between-group difference (unadjusted for baseline): -1.6 (95% CI, -9.8 to 6.6); *P* = 0.69 Calculated between-group difference (adjusted for baseline): 2.7 (*P* value not calculable)
	Ways of Coping Check List Revised No	Problem-focused subscale, mean score (SD), N Baseline Information: 14.4 (11.2), 28 Information + sound: 8.8 (7.9), 20 12 mo. Information: 14.5 (10.0), 17 Information + sound: 15.9 (12.1), 12 Calculated between-group difference (unadjusted for baseline): 1.4 (95% CI, -7.0 to 9.8); *P* = 0.74 Calculated between-group difference (adjusted for baseline): 7.0 (*P* value not calculable)
	Derogatis Stress Profile No	Mean score (SD), N Baseline Information:119.2 (32.0), 28 Information + sound: 119.3 (27.1), 20 12 mo. Information: 112.4 (36.7), 17 Information + sound: 123.4 (29.4), 12 Calculated between-group difference (unadjusted for baseline): 11 (95% CI, -15.2 to 37.2); *P* = 0.40 Calculated between-group difference (adjusted for baseline): 10.9 (*P* value not calculable)
Henry et al. (2017)[16] Hearing aid (HA) (18) Hearing aids with sound generator (HA+SG) (19)	Tinnitus Functional Index Yes	Between-group difference, 4 to 5 months; N: -12.5 (SE 5.7), *P* = 0.079 N (%) with clinically significant TFI reduction (≥13-points) HA: 12* (67) HA+SG: 15* (79) *P** = 0.21
Henry et al. (2015)[189]	Tinnitus Functional	Mean change in score at 3 months

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Not sure)	Results
Hearing aid control (15) Hearing aid + sound Generator (15)	Index Yes	Control: -32.9 Sound: -39.3 Between-group difference in mean score at 3 wks*: -6.4 N (%) with clinically significant TFI (≥13 points) improvement at 3 mos Control: 13 (87) Sound: 13 (87) *P* = 0.99* RD* 0% (95% CI, -24.3% to 24.3%) RR* 1.0 (95% CI, 0.76 to 1.3)
Hiller et al. (2005)[23] Tinnitus education or CBT (69) Tinnitus education or CBT Plus sound generator (67)	Tinnitus Questionnaire Not sure	Mean (SD) score at baseline; N Education: 24.4 (9.0); 33 Education + Sound: 26.9 (10.7); 31 Mean (SD) score immediately after treatment; N Education: 14.5 (9.0), 33 Education + Sound:: 17.9 (9.3), 31 Between-group difference in mean change in score: NR; *P* = NS Mean (SD) score at 6 mos; N Education: 13.4 (9.9), 31 Education + Sound:: 17.2 (7.9), 28 Between-group difference in mean change in score: NR; *P* = NS Mean (SD) score at 18 mos; N Education: 14.3 (8.9), 28 Education + Sound: 17.4 (9.3), 29 Between-group difference in mean change in score: NR; *P* = NS Mean (SD) score at baseline; N CBT: 48.8 (12.8; 29 CBT+ Sound: 53.4 (12.4); 31 Mean (SD) score immediately after treatment; N CBT: 36.1 (15.7), 33 CBT + Sound:: 42.9 (18.7), 31 Between-group difference in mean change in score: NR; *P* = NS Mean (SD) score at 6 mos; N CBT: , 31.8 (17.4); 24 CBT + Sound:: 38.6 (18.9), 27 Between-group difference in mean change in score: NR; *P* = NS Mean (SD) score at 18 mos; N CBT: 27.5 (16.4), 22

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Not sure)	Results
		CBT + Sound: 37.8 (18.6)), 26 Between-group difference in mean change in score: NR; *P* = NS
	VAS for tinnitus loudness Not sure	Mean (SD) score at baseline; N Education: 43.6 (13.6); 30 Education + Sound: 49.5 (20); 31 Mean (SD) score immediately after treatment; N Education: 33.4 (20.9), 30 Education + Sound: 40.3 (18.8), 31 Between-group difference in mean change in score: NR; *P* = NS Mean (SD) score at 6 mos; N Education: 28.8 (20.3), 27 Education + Sound: 43.9 (22.3), 27 Between-group difference in mean change in score: NR; *P*<0.05 favoring control Mean (SD) score at baseline; N CBT: 55.6 (15.9); 23 CBT + Sound: 56.7 (18.1); 30 Mean (SD) score immediately after treatment; N CBT: 46.7 (20.6) 23 CBT + Sound: 52.0 (20.8), 30 Between-group difference in mean change in score: NR; *P* = NS Mean (SD) score at 6 mos; N CBT: 50.0 (22.8), 21 CBT + Sound: 53.1 (24.7), 26 Between-group difference in mean change in score: NR; *P* = NS
	VAS for tinnitus control Not sure	Mean (SD) score at baseline; N Education: 20.4 (18.3); 28 Education + Sound: 27.9 (25.3); 30 Mean (SD) score immediately after treatment; N Education: 27 (21.5), 28 Education + Sound: 32.4 (28.7), 30 Between-group difference in mean change in score: NR; *P* = NS Mean (SD) score at 6 mos followup; N Education: 28.2 (28.6), 26 Education + Sound: 29.1 (25.6), 27 Between-group difference in mean change in score: NR; *P* = NS Mean (SD) score at baseline; N CBT: 24.4 (20.1); 21

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Not sure)	Results
		CBT + Sound: 25.3 (18.7); 30 Mean (SD) score immediately after treatment; N CBT: 42.4 (29.1) 21 CBT + Sound: 44.1 (26.0), 30 Between-group difference in mean change in score: NR; *P* = NS Mean (SD) score at 6 mos followup; N CBT:3 3.1 (28.3), 20 CBT+ Sound: 40.8 (23.2), 25 Between-group difference in mean change in score: NR; *P* = NS
	VAS-unpleasantness Not sure	Mean (SD) score at baseline; N Education: 25.3 (14.5); 28 Education + Sound: 30.2 (18.3); 31 Mean (SD) score immediately after treatment: N Education: 24 (20), 28 Education + Sound: 23.9 (17.1), 31 Between-group difference in mean change in score: NR; *P* = NS Mean (SD) score at 6 mos followup; N Education: 18.8 (19.3), 26 Education + Sound: 24.5 (17.6), 27 Between-group difference in mean change in score: NR; *P* = NS Mean (SD) score at baseline; N CBT 43.0 (17.9); 23 CBT + Sound: 44.3 (19.0); 30 Mean (SD) score immediately after treatment: N CBT: 37.6 (20.6), 23 CBT + Sound: 40.3 (20.3); 30 Between-group difference in mean change in score: NR; *P* = NS Mean (SD) score at 6 mos followup; N CBT: 37.7 (24.2), 21 CBT + Sound: 41.2 (23.5), 26 Between-group difference in mean change in score: NR; *P* = NS
Li et al. (2016)[17] Control music (25) Altered music (25)	Tinnitus Handicap Inventory Yes	Mean (SE) between-group difference in change in score; ES; N 3 mo.: -12.8 (4.4), *P* = 0.0008; ES = 0.61; 19 control; 14 treatment 6 mo.: -14.9 (4.2), *P* = 0.0001; ES = 0.58; 17 control; 14 treatment 1 y: -17.4 (4.4), *P* = 0.0001; ES = 0. 60; 16 control; 12 treatment
	Tinnitus Functional Index	Mean (SE) between-group difference in change in score at 3 mo.: -2.1 (5.2), *P* = 0.69; 19 control; 14 treatment Mean (SE) between-group difference in change in score at 6 mo.: -7.6 (3.7), *P* = 0.048; ; 17 control; 14 treatment

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Not sure)	Results
	No	Mean (SE) between-group difference in change in score at 1 y.: -5 (6.0), *P* = 0.41; 16 control; 12 treatment
	Hospital Anxiety and Depression Scale-Depression No	Mean (SE) between-group difference in change in score at 6 mo.: -.6 (1.0); *P* = 0.546; ; 17 control; 14 treatment Mean (SE) between-group difference in change in score at 1 y.: 0.1 (0.9); *P* = 0.88; 16 control; 12 treatment
	Hospital Anxiety and Depression Scale-Anxiety No	Mean (SE) between-group difference in change in score at 6 mo.: -2.7 (1.0); *P* = 0.013; ; 17 control; 14 treatment Mean (SE) between-group difference in change in score at 1 y.: -1.2 (1.3); *P* = .345; 16 control; 12 treatment
Okamoto et al. (2010)[22] Placebo music (13) Monitoring (13) Notched music (13)	VAS for tinnitus loudness Not sure	Between-group difference notched music vs. placebo over 1 to 6 months; NR Between-group difference target vs. placebo over 7 to 12 months; *P* = 0.03 favoring notched music
Schad et al. (2018)[15] Placebo (10) Notched noise (10) Matched noise (10)	Tinnitus Functional Index No	Mean (SE) change in score at 2 weeks Placebo: -6.86 (3.46) Notched: -14.67 (3.29) Matched: -11.42 (3.29) Notched v. Placebo, between-group difference: -7.8 (95% CI,* -17.8 to 2.2), *P* = 0.12* Matched v. Placebo, between-group difference: -4.6 (95% CI*, -14.6 to 5.5), *P* = .35* TFI Mean (SE) change from baseline to 4 weeks: Placebo: -12.78 (3.46) Notched: -17.14 (3.43) Matched: -10.88 (3.29) Notched v. Placebo, between-group difference* : -4.4 (95% CI, -14.6 to 5.9), *P* = .38 Matched, v. Placebo, between-group difference*: -1.9 (95% CI, -8.1 to 11.9), *P* = 0.70
	VAS for tinnitus loudness No	Mean (SE) change in score at 2 weeks Placebo: -0.29 (0.54) Notched: -1.05 (0.51) Matched: -0.57 (0.51) Notched v. placebo, between-group difference: -0.76 (95% CI*, -2.3 to 0.8), *P** = 0.32 Matched v. placebo, between-group difference: -0.28 (95% CI*, -1.8 to 1.3), *P** = 0.71 Mean (SE) change in score at 4 weeks Placebo: -1.50 (0.54) Notched: -0.63 (0.54) Matched: -0.59 (0.51) Notched v. placebo, between-group difference: 0.87 (95% CI*, -0.7 to 2.5), *P** = 0.27 Matched v. placebo, between-group difference: 0.91 (95% CI*, -0.7 to 2.5), *P** = 0.24

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Not sure)	Results
Stein et al. (2016)[20] Placebo (50) Tailor-made notched music training (50)	Tinnitus Handicap Questionnaire Yes	Mean difference in score with repeated measures at the end of 3 mos of treatment: NR; *P* = 0.869 (ITT) Mean difference in score with repeated measures 1 mo after treatment conclusion: NR; *P* = 0.305 (Per protocol)
	VAS total score calculated by average score of VAS for loudness, annoyance, awareness, and handicap Yes	Mean difference in score with repeated measures at the end of 3 mos of treatment: NR; *P* = 0.390 (ITT) Mean difference in score with repeated measures 1 mo after treatment conclusion: NR; *P* = 0.182 (per protocol)
Strauss et al. (2015)[21] Hearing aid control (10) Hearing aid + notched environmental sound technology (10)	Mini-TQ No	Between-group difference at 3 weeks Results only reported on figure, actual values and *P* value NR, confidence intervals are overlapping. Cohen's d effect size: 0.84 (95% CI, NR)
Wise et al. (2016)[18] Control game (16) Terrain game(15)	Tinnitus Handicap Inventory No	Mean change in score over time to 3 weeks post-intervention Between-group difference NR: *P*< 0.01 favoring terrain
	Tinnitus Functional Index Yes	Mean change in score over time to 3 weeks post-intervention Between-group difference NR: *P* = 0.072 N (%) TFI significant improvement (>13 points) Control game: 4 (25*) Terrain: 9 (60*) *P** = 0.06 RD* 35.0% (95% CI, 2.4% to 67.3%) RR* 2.4 (95% CI, 0.94 to 6.2)
	Tinnitus Severity Scale No	Tinnitus Severity Numeric Scale (TSNS) "Ability to ignore tinnitus": Mean change in score over time to 3 weeks post-intervention Between-group difference NR: *P*< 0.01 All other TSNS scales (annoying unpleasant, uncomfortable, and loudness) had no significant between-group differences.

Notes: * Indicates a data value that we calculated based on data provided in the publication.

Abbreviations: CBT = cognitive behavioral therapy; CI = confidence intervals; ES = effect size; HA = hearing aid; HA+SG = hearing aid with sound-generating feature; mo. = month(s); N = number of participants; NR = not reported; NS = not significant; RD = risk difference; RR = risk ratio; SD = standard deviation; SE = standard error; TFI = Tinnitus Functional Index; w = week(s); y = year(s).

Table D1e. Safety and Cost Outcomes for Sound Therapy Interventions

Authors (Year) Interventions (N Randomized)	Safety Outcomes	Cost Outcomes
Davis et al. (2008)[24] Counseling only (13) Neuromonics (22) Sound + counseling (15)	NR	NR
Dineen et al. (1999)[19] Dineen et al. (1997)[190] Dineen et al. (1997)[25] Information only (28) Information with sound device (20)	NR	NR
Henry et al. (2017)[16] Hearing aid (18) Hearing aids with sound generator (19)	NR	NR
Henry et al. (2015)[189] Hearing aid control (15) Hearing aid + sound generator (15)	NR	NR
Hiller et al. (2005)[23] Tinnitus education or CBT (69) Tinnitus education or CBT plus sound generator (67)	NR	NR
Li et al. (2016)[17] Control music (25) Altered music (25)	NR	NR
Okamoto et al. (2010)[22] Placebo music (13) Monitoring (13) Notched music (13)	NR	NR
Schad et al. (2018)[15] Placebo (10) Notched noise (10) Matched noise (10)	NR	NR
Stein et al. (2016)[20] Placebo (50) Tailor-made notched music training(50)	N (%) of patients who reported harms: Placebo: 15 (30.0*) Music training: 12 (24*) Harms reported included increased loudness, additional tinnitus sounds, more awareness of tinnitus sound, occasionally louder tinnitus sound, change in sense of hearing,	NR

Strauss et al. (2015)[21] Hearing aid control (10) Hearing aid + notched environmental sound technology(10)	NR	NR
Wise et al. (2016)[18] Control game (16) Terrain game (15)	NR	NR

Notes: * Indicates a data value that we calculated based on data provided in the publication.

Abbreviations: CBT = cognitive behavioral therapy; N = number of participants; NR = not reported.

Table D2a. Study Characteristics for Included Repetitive Transcranial Magnetic Stimulation Interventions

Authors (Year)	Study Design	Sponsor	Country	Eligible Study Arms	Total N Overall/ Total N in Eligible Study Arms	Risk of Bias
Anders et al. (2010)[26]	RCT	Research grants	Czech Republic	Sham rTMS rTMS	52/ 52	High
Barwood et al. (2013)[27]	RCT	Estate of Dulcie Rose Gardner	Australia	Sham rTMS rTMS	8/ 8	High
Chung et al. (2012)[28]	RCT	China Medical University, China Medical University Hospital, the Clinical Trial and Research Center of Excellence Funds, and the National Science Council from Taiwan's Department of Health.	Taiwan	Sham rTMS rTMS	22/ 22	Some concerns
Folmer et al. (2015)[29]	RCT	U.S. Department of Veterans Affairs Rehabilitation Research and Development Service and Veterans Affairs National Center for Rehabilitative Auditory Research at Portland Veterans Affairs Medical Center.	U.S.	Sham rTMS rTMS	70/ 70	Some concerns
Formanek et al. (2018)[30]	RCT	Ministry of Health, Czech Republic	Czech Republic	Sham rTMS rTMS	53/ 22	Some concerns
Hoekstra et al. (2013)[31]	RCT	NR	The Netherlands	Sham rTMS rTMS	52/ 52	Some concerns
Kleinjung et al. (2005) et al.[36] Langguth et al. (2007)[191]	Crossover RCT	Tinnitus Research Initiative	Germany	Sham rTMS rTMS	10/ 10	Some concerns
Landgrebe et al. (2017)[32]	RCT	German Research Foundation	Germany	Sham rTMS rTMS	153/ 153	Low
Mennemeier et al. (2011)[37]	Crossover RCT	NIH National Center for Research Resources Centers of Biomedical Research Excellence (COBRE); National Institute of Neurological Disorders and Stroke; National Institute of Child Health and Human Development; and a Tinnitus Research Consortium Grant-in-Ai	U.S.	Sham rTMS rTMS 1 Hz	21/ 21	Some concerns
Piccirillo et al. (2013)[38]	Crossover RCT	National Institutes of Deafness and Other Communication Disorders	U.S.	Sham rTMS rTMS	20/ 20	High
Piccirillo et al. (2011)[39]	Crossover RCT	National Institutes of Deafness and Other Communication Disorders	U.S.	Sham rTMS rTMS 1 Hz	14/ 14	Some concerns
Plewnia et al. (2012)[33]	RCT	German Research Council	Germany	Sham rTMS Secondary auditory cortex rTMS	48/ 48	Some concerns
Plewnia et al.	Crossover	American Tinnitus Association and the University of	Germany	Sham rTMS	6/	Some

Authors (Year)	Study Design	Sponsor	Country	Eligible Study Arms	Total N Overall/ Total N in Eligible Study Arms	Risk of Bias
(2007)[40]	RCT	Tuebingen		rTMS 1 Hz	6	concerns
Rossi et al. (2007)[41]	Crossover RCT	NR	Italy	Sham rTMS rTMS 1 Hz	16/ 16	Some concerns
Sahlsten et al. (2017)[34]	RCT	Finnish Governmental University Hospital grants, Finnish Research Foundation of Ear Diseases, and State research funding from the Hospital District of Southwest Finland.	Finland	Sham rTMS rTMS	42/ 42	Some concerns
Schecklmann et al. (2016)[35]	RCT	No third-party funding	Germany	Sham cTBS cTBS	23/ 23	Some concerns
Vanneste et al. (2012)[42]	Crossover RCT	NR	Belgium	Study 1 Sham rTMS Study 1 rTMS 1 Hz	60/ 60	High
Vanneste et al. (2012)[43]	Crossover RCT	NR	Belgium	Study 1 Sham rTMS Study 1 rTMS 1-Hz	64/ 64	Some concerns
Vanneste et al. (2011)[44]	Crossover RCT	NR	Belgium	Sham rTMS rTMS 1 Hz	78/ 78	High

Abbreviations: Hz = electromagnetic wavelength frequency; NR = note reported; RCT = randomized controlled trial; rTMS = repetitive transcranial magnetic stimulation; cTBS = continuous theta-burst stimulation, a variation of rTMS.

Table D2b. Population Characteristics For Included Repetitive Transcranial Magnetic Stimulation Interventions

Authors (Year)	Study Population	Mean age (SD)	N (% Female)	N (%) Race/Ethnicity	Other characteristics
Anders et al. (2010)[26]	Adults with chronic, treatment-resistant tinnitus of > = 6 months in duration recruited from outpatients seeking treatment at a university otolaryngology clinic *Inclusion:* Age 18 to 70 years with chronic tinnitus > = 6 months duration, pharmacological treatment for > = 3 months duration without significant clinical response, rTMS-naive, age-adjusted normal sensorineural hearing, a normal neurological exam, normal cranial magnetic resonance imaging finding, and normal middle ear status. *Exclusion:* Concurrent other forms of tinnitus treatment, a history of neuropsychiatric disorder, pacemaker and other metal implants, implanted medication pump, pregnancy, lactation, presence of other significant medical condition, concomitant psychotropic medication or medication that lowers seizure threshold or reduced cortical excitation, concomitant axis I psychiatric disorders according to ICD-10, or participation in a clinical trial with the prior 30 days.	Sham rTMS: 50.1 (14.0) rTMS: 48.1 (14.9)	13 (31.0)	NR	*Tinnitus Duration* Mean (SD) duration in months Sham rTMS: 88.4 (67.5) rTMS: 106.8 (81.6) *Hearing Loss* Persons with hearing loss were explicitly excluded
Barwood et al. (2013)[27]	Adults with bilateral, chronic tinnitus > = 1 year in duration recruited from an advertisement on a university staff information system. *Inclusion:* Adults with bilateral, chronic tinnitus >1 year in duration with no self-reported neurological or psychological conditions; normal hearing thresholds < = 3,000 Hz or hearing losses ranging from mild to severe >3,000 Hz according to the Goodman classification system. *Exclusion:* History of seizures or epilepsy, neurological disorders, brain injury, cardiac pacemakers, metal implants or implanted medication pumps; and taking mood altering medications including antidepressants or neuroepileptic medications.	42.4 (8.8*)	4 (50)	NR	*Tinnitus Duration* Mean (SD) in years 14 (10.2)* *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled
Chung et al. (2012)[28]	Adults with chronic tinnitus > = 6 months in duration. *Inclusion:* Adults, right-handed, with symptoms that	53.0 (16.8)	2 (9.1)	NR	*Tinnitus Duration* Mean (SD) duration in years: 6.6 (5.6)

Authors (Year)	Study Population	Mean age (SD)	N (% Female)	N (%) Race/Ethnicity	Other characteristics
	had not resolved with medication or other adjuvant treatments such as acupuncture and retraining therapy. *Exclusion:* Patients with narrow band, white or pink tinnitus; known history of metal implantation, head injury, stroke, or epilepsy.				*Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled
Folmer et al. (2015)[29]	Adults with chronic tinnitus > = 1 year in duration recruited from the community. *Inclusion:* Adults, 18 years or older, with constant chronic tinnitus greater than or equal to 1 year in duration., with self-rated tinnitus 6 or greater on a 0 to 10 scale. All degrees on hearing function included and a 4-week washout from any other tinnitus treatment or management program was required prior to entering this study. *Exclusion:* Objective tinnitus, history of seizures or epileptic activity, history or evidence of significant brain malformation or neoplasm; cerebral vascular events (such as strokes), prior brain surgery, cardiac pacemakers, other electronic implants (including cochlear implants), drugs that might reduce the seizure threshold, and pregnancy.	Placebo: 62.8 (8.3) rTMS: 58.3 (9.5)	13 (20.3)	NR	*Tinnitus Duration* N (%) with duration of tinnitus 1-2 y Placebo: 2 (6.2*) rTMS: 4 (12.5*) 3-5 y Placebo: 3 (9.4) rTMS: 6 (18.8*) 6-10 y Placebo: 3 (9.4) rTMS: 5 (15.6*) 11-20 y Placebo: 4 (12.5*) rTMS: 9 (28.1*) >20 y Placebo: 20 (62.5*) rTMS: 8 (25*) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled
Formanek et al. (2018)[30]	Adults with chronic subjective primary tinnitus *Inclusion:* Unilateral or bilateral chronic subjective nonpulsatile primary tinnitus for at least 6 months *Exclusion:* Head injury or brain surgery, epilepsy, organic brain lesion, Meniere's disease or fluctuating hearing loss, cochlear or bone-anchored hearing device implantation, history of attempted suicide, pregnancy, consumption of anticonvulsants or antipsychotic medication, pacemaker, or previous rTMS	Sham: 51.8 (10.3) rTMS: 47.9 (14.3)	9 (28.1)	NR	*Tinnitus Duration* Mean (SD) in months Sham: 76.8 (76.9) rTMS: 53.4 (61.9) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled
Hoekstra et al.	Patients with nonfluctuating tinnitus > = 2 months	52 (12)	9 (18)	NR	*Tinnitus Duration*

Authors (Year)	Study Population	Mean age (SD)	N (% Female)	N (%) Race/Ethnicity	Other characteristics
(2013)[31]	duration recruited from a university-based tinnitus clinic *Inclusion:* Nonfluctuating tinnitus of at least 2 months duration *Exclusion:* Patients with a treatable cause of their tinnitus (e.g. cerumen) or psychiatric disease; use of anticonvulsant or psychotherapeutic medication that lowers seizure thresholds; history of or family members with epilepsy, migraine, structural brain changes, severe internal or heart disease, alcohol or drug abuse; irremovable metal objects in the body; metal workers; and pregnancy.				Duration (range) in months 46 (8 to 420) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled
Kleinjung (2005)[36] Langguth et al. (2007)[191]	Patients with chronic tinnitus *Inclusion:* Patients with mild to severe unilateral or bilateral chronic tinnitus of at least 6 months duration *Exclusion:* Concomitant anticonvulsant drug treatment, unilateral hearing loss, or middle ear pathologies	47.6 (13.4)	2 (20)	NR	*Tinnitus Duration* Mean (SD) tinnitus duration in years: 3.9 (3.3) *Hearing Loss* Patients with unilateral hearing loss were excluded
Landgrebe et al. (2017)[32]	Adults with at least moderate-severity chronic tinnitus > = 6 months duration *Inclusion:* Age 18 to 70 years, chronic tinnitus for at least 6 months with at least moderate severity defined as a score on the THI of at least 38 points and normal hearing and naïve to rTMS. *Exclusion:* Objective tinnitus, simultaneous tinnitus-specific treatments, clinically relevant psychiatric comorbidity, simultaneous treatment with psychotropic agents, severe unstable somatic comorbidity, contraindications for rTMS, pregnancy and participation in a clinical trial within the last 30 days.	Sham: 49.9 (13.2) rTMS: 48.1 (12.5)	41 (28.1)	NR	*Tinnitus Duration* Sham: 8.1 (8.4) rTMS: 6.2 (5.3) *Hearing Loss* Persons with hearing loss were explicitly excluded
Mennemeier et al. (2011)[37]	Adults with chronic bilateral tinnitus >6 months in duration recruited from a hearing and balance clinic. *Inclusion:* Adults 28 to 75 years of age with chronic bilateral tinnitus >6 months in duration, completing and passing the Transcranial Magnetic Stimulation Adult Safety Screen, and having a CT or MRI scan showing no brain abnormality. Individuals taking	NR	NR	NR	*Tinnitus Duration* NR *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled

Authors (Year)	Study Population	Mean age (SD)	N (% Female)	N (%) Race/Ethnicity	Other characteristics
	SSRIs for depression related to tinnitus had to be stable on doses of the medications for 3 months and could not change medications during the duration of the study. *Exclusion:* A history of epilepsy, head injury, aneurysm, stroke, previous cranial neurosurgery, acoustic neuroma or glomus tumor; active Meniere's disease; diagnosis of a neurological or major psychiatric disorder (excluding depression or anxiety); metal implants in the head or neck or a pacemaker; pregnancy; or currently taking medications that lower seizure threshold or reduce cortical excitation.				
Piccirillo et al. (2013)[38]	Adults with subjective, unilateral or bilateral, nonpulsatile tinnitus > = 6 months duration recruited from a research registry or an online website. *Inclusion:* Adults between the ages of 18 and 60 years with subjective, unilateral or bilateral, nonpulsatile tinnitus > = 6 months duration and a score of 30 or greater on THI. *Exclusion:* NR	Median 42 (range 22 to 59)	5 (36)	White: 11 (79) Black: 2 (14) Other: 1 (7)	*Tinnitus Duration* Median (IQR) duration in years: 8.0 (IQR 0.1 to 30) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled
Piccirillo et al. (2011)[39]	Adults with chronic tinnitus > = 6 months in duration. *Inclusion:* Adults 18-60 years old with subjective, unilateral or bilateral, nonpulsatile chronic tinnitus with a duration of 6 months or longer; score of > = 38 on THI ; score of <14 on BDI *Exclusion:* Those with clinical depression (> = 14 on the BDI) or other psychiatric or neurological disorders.	Median 52	4 (29)	White: 13 (93) Other (Native American, nonwhite): 1 (7)	*Tinnitus Duration* Median (IQR) duration of tinnitus in years: 7.0 (0.5 to 17.9) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled
Plewnia et al. (2012)[33]	Adults with chronic subjective tinnitus <5 years in duration recruited via public media advertisements and outpatient otolaryngology clinics. *Inclusion:* Adults with a less than 5 years history of chronic subjective tinnitus. *Exclusion:* Objective tinnitus; acute or chronic inflammation of the middle ear; sudden idiopathic hearing loss or hearing loss due to an acute acoustic trauma within the last 6 weeks; Meniere disease or fluctuating hearing loss; or history of seizures, brain trauma, brain surgery, heart pacemaker, intake of	Sham rTMS: 45.6 (10.3) Secondary auditory cortex rTMS: 46.4 (13.0) Tempoparietal association cortex rTMS: 55.8 (9.7)	23* (47.9)*	NR	*Tinnitus Duration* Mean (SD) duration in months Sham rTMS: 22 mo (14) Secondary auditory cortex rTMS: 27 mo (14) Tempoparietal association cortex rTMS: 28 mo. (13) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled

Authors (Year)	Study Population	Mean age (SD)	N (% Female)	N (%) Race/Ethnicity	Other characteristics
	anticonvulsants, antipsychotics, or benzodiazepines.				
Plewnia et al. (2007)[40]	Adults with chronic, bilateral tinnitus >1 year in duration recruited because participation in a prior PET/rTMS study *Inclusion:* No additional criteria specified. *Exclusion:* Adults with heart disease, history of seizure or brain lesions, metal implants, cardiac pacemaker and current use of psychotherapeutic drugs.	57.7* (5.9*)	1 (17*)	NR	*Tinnitus Duration* Mean (SD) duration in years 5.7* (3.1*) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled
Rossi et al. (2007)[41]	Adults with chronic tinnitus >1 year in duration *Inclusion:* Adults with chronic, mono- or bilateral tinnitus >1 year in duration with normal neurological examination and normal cranial magnetic resonance *Exclusion:* History of neuropsychiatric disorders or neuroactive treatments (with the exception of antidepressant therapy previously taken for tinnitus therapy, withdrawn for at least 1 month), and presence of significant other medical illness	52.5 (10.6)	3 (21)	NR	*Tinnitus Duration* Mean (SD) duration in years: 8 (7.4) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled *Other* N (%) with noise trauma: 1 (7)
Sahlsten et al. (2017)[34]	Adults with chronic tinnitus of 6 months-10 years duration recruited from a University hospital. *Inclusion:* Age 18 to 65 years, with uni- or bilateral chronic tinnitus of 6 months to 10 years duration. Tinnitus intensity VAS at least 4 of 10. *Exclusion:* Pulsatile tinnitus, objective tinnitus, magnetically active, metallic intra-corporeal appliances (e.g. cochlear implants and cardiac pacemakers), epilepsy or increased risk of seizure (e.g. brain tumor, stroke, alcohol abuse), active bipolar disorder, severe heart disease, migraine, prior rTMS treatment, and pregnancy.	Placebo: 51.5 (10.7)# rTMS: 48.9 (13.1)# #for N Analyzed	12 (31)# #for N Analyzed	NR	*Tinnitus Duration* Mean (SD) duration in years Placebo: 4.9 (2.7) rTMS: 5.4 (2.5) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled
Schecklmann et al. (2016)[35]	Adults with chronic tinnitus *Inclusion:* Chronic tinnitus (undefined) *Exclusion:* Acute or chronic inflammation of the middle ear, Meniere disease, sudden idiopathic hearing loss or fluctuating hearing, a history of seizures, a suspected diagnosis of organic brain damage, pregnancy as well as patients with cardiac pacemakers, mobile metal implants or implanted	Sham: 46.5 (11.5) cTBS: 48.2 (10.7)	9 (39)	NR	*Tinnitus Duration* Mean (SD) duration in months Sham: 96.8 (120.4) cTBS: 68.9 (61.4) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled

Authors (Year)	Study Population	Mean age (SD)	N (% Female)	N (%) Race/Ethnicity	Other characteristics
	medication pumps.				
Vanneste et al. (2012)[42]	Adults with chronic unilateral or bilateral tinnitus >1 year duration. *Inclusion:* NR *Exclusion:* NR	50.1 (11.8)	24 (40*)	NR	*Tinnitus Duration* Mean (SD) in years: 8.3 (9.5) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled
Vanneste et al. (2012)[43]	Adults with chronic unilateral or bilateral tinnitus >1 year duration recruited from an outpatient university hospital tinnitus clinic. *Inclusion:* Adults with unilateral or bilateral chronic tinnitus >1-year duration. *Exclusion:* NR	Study 1: 52.2 (9.8) Study 2: 53.7 (7.6)	Study 1: 11 (46)* Study 2: 16 (40)*	NR	*Tinnitus Duration* Mean (SD) duration in years Study 1: 9.1 (8.4) Study 2: 7.1 (3.2) *Hearing Loss* Hearing loss was not required or excluded, and no mention of this characteristic was made in describing the study population
Vanneste et al. (2011)[44]	Adults with chronic unilateral or bilateral tinnitus recruited from a multidisciplinary university tinnitus clinic *Inclusion:* Adults with chronic unilateral or bilateral tinnitus who underwent a complete audiological, ENT and neurological investigation to rule out possible treatable causes for their tinnitus. *Exclusion:* Adults with treatable causes for their tinnitus	53.5 (11.9)	15 (19.2)*	NR	*Tinnitus Duration* Mean (SD) duration in years: 7.8 (SD 8.4) *Hearing Loss* Hearing loss was not required or excluded, and no mention of this characteristic was made in describing the study population

Notes: * Indicates a data value that we calculated based on data provided in the publication. # Indicates that the data was only reported for study completers, not the N that was randomized.

Abbreviations: CTBS: continuous theta burst stimulation, a variation of rTMS; IQR: interquartile range; NR = not reported; rTMS = repetitive transcranial magnetic stimulation; SD: standard deviation.

Table D2c. Intervention Characteristics for Included Repetitive Transcranial Magnetic Stimulation Interventions

Authors (Year)	Duration of Intervention	Control Group (N randomized or enrolled)	Intervention Group(s) (N randomized or enrolled)	Fidelity
Anders et al. (2010)[26]	2 weeks	**Sham rTMS (26)** Magstim Super Rapid with figure-of-eight coils administered over the left auditory cortex. Patients in the sham group received the same treatment as the active rTMS group, but with a sham stimulation coil. Patients received 5 sessions on 5 consecutive business days.	**rTMS (26)** Active rTMS (1 Hz) with Magstim Super Rapid stimulator, 1,500 stimuli per session on 2 x 5 sessions with a stimulation intensity of 110% of the individual resting motor threshold, figure-of-eight coil positioned over the left primary auditory cortex. Patients received 5 sessions on 5 consecutive business days.	All but 10 completed all sessions
Barwood et al. (2013)[27]	10 days	**Sham rTMS (4)** Placebo rTMS (1 Hz) with Magstim Rapid2 stimulator, 2,000 pulses per daily session on 10 consecutive workdays with a stimulation intensity of 110% or lower related to the individual resting motor threshold, placebo figure-of-eight coil positioned over the left auditory cortex; the placebo coil was a sham coil that presented a sound only with no magnetic pulse administered at each stimulus event.	**rTMS (4)** Active rTMS (1 Hz) with Magstim Rapid2 stimulator, 2,000 pulses per daily session on 10 consecutive workdays with a stimulation intensity of 110% related to the individual resting motor threshold, figure-of-eight coil positioned either over the left auditory cortex.	All completed the 10 sessions.
Chung et al. (2012)[28]	10 days	**Sham rTMS (10)** Magstim SuperRapid with figure-eight coil placed on the surface of the skull over the targeted region (orthogonal projection of the auditory cortex). Patients in the sham group received the same treatment as the active rTMS group, but with a sham coil.	**rTMS (12)** Magstim SuperRapid with figure-eight coil placed on the surface of the skull over the targeted region (orthogonal projection of the auditory cortex) with the intensity at 80% of the resting motor threshold. A burst frequency of 5 Hz applied with 900 pulses of theta-burst rTMS delivered daily for 10 business days.	NR
Folmer et al. (2015)[29]	2 weeks	**Placebo rTMS (35)** Placebo rTMS (1 Hz) with Magstim Rapid2 stimulator, 2,000 pulses per daily session on 10 consecutive workdays with a stimulation intensity of 110% or lower related to the individual resting motor threshold, placebo figure-of-eight coil positioned either over the left (N = 16) or right (N = 16) auditory cortex; the placebo coil included a metal plate which blocks the magnetic field generated.	**rTMS (35)** Active rTMS (1 Hz) with Magstim Rapid2 stimulator, 2,000 pulses per daily session on 10 consecutive workdays with a stimulation intensity of 110% or lower related to the individual resting motor threshold, figure-of-eight coil positioned either over the left (N = 16) or right (N = 16) auditory cortex.	All but 3 participants completed at least 9 of the 10 sessions.

Authors (Year)	Duration of Intervention	Control Group (N randomized or enrolled)	Intervention Group(s) (N randomized or enrolled)	Fidelity
Formanek et al. (2018)[30]	5 days	**Sham rTMS (12)** DuoMAG XT-100 transcranial magnetic stimulator with 70-mm 70 BFP Placebo Butterfly Coil replcating the appearance, sound emission, stimulation of superficial tissue, and operation of the real coil without stimulating the cortical tissue.	**rTMS (20)** DuoMAG XT-100 transcranial magnetic stimulator with 70-mm air-cooled 70BF Butterfly Coil; intensity set according to rmt (dorsolateral prefrontal cortex, frequency 25 Hz, 300 pulses, 80% RMT on the left side and primary auditory cortex, 1 Hz, 1,000 pulses, 110% RMT) on both sides. Stimulation for 5 consecutive days, 2,300 pulses per session of three stimulation sites.	NR
Hoekstra et al. (2013)[31]	5 days	**Placebo (24)** Same as rTMS intervention except for use of a placebo coil.	**rTMS (26)** Magstim Rapid2 magnetic stimulator with an air-cooled 70-mm figure-of-eight coil at an intensity of 110% of the patient's motor threshold. 1-Hz-rTMS applied for 2,000 pulses to each auditory cortex. Stimulation received on 5 consecutive days.	All but 1 patient completed all sessions.
Kleinjung et al. (2005)[36] Langguth (2007)[191]	5 days	**Sham rTMS (10)** Active rTMS (1 Hz) with Magstim stimulator and specific sham-coil system positioned over the auditory cortex; patients received 2,000 pulses per daily session on 5 consecutive workdays with a stimulation intensity of 110% of motor threshold.	**rTMS (10)** Active rTMS (1 Hz) with Magstim stimulator and figure-of-eight coil positioned over the auditory cortex; patients received 2,000 pulses per daily session on 5 consecutive workdays with a stimulation intensity of 110% of motor threshold	All patients completed the study
Landgrebe et al. (2017)[32]	2 weeks	**Sham rTMS (75)** MagPro X-100 or MagPro R30 with passively-cooled MCF-B65 figure-of-eight coils. Patients in the sham group received the same treatment as the active rTMS group, but the stimulation coil was tilted away from the skull by 45 degrees with one wing touching the skull.	**rTMS (71)** MagPro X-100 or MagPro R30 with passively-cooled MCF-B65 figure-of-eight coils. 1 -Hz-rTMS applied to the left primary auditory cortex with a stimulation intensity of 110%. Stimulation received 10 sessions total (daily sessions over 2 weeks), 2,000 stimuli per session.	Sham: 4 (5.3%) participants did not complete the whole treatment period rTMS: 1 (1.4%) participants did not complete the whole treatment period
Mennemeier et al. (2011)[37]	1 week	**Sham rTMS (21)** Magstim Super Rapid stimulator with Magstim air-film, figure-of-eight coil used to deliver stimulation. Five-day course of sham 1-Hz rTMS with 1800 pulses at 110% of motor threshold to the temporal cortex. Sham stimulation was delivered using a visually identical sham coil but delivers only 5% of the maximum stimulator output.	**rTMS 1 Hz (21)** Magstim Super Rapid stimulator with Magstim air-film, figure-of-eight coil used to deliver stimulation. Five-day course of active 1-Hz rTMS with 1800 pulses at 110% of motor threshold to the temporal cortex.	NR

Authors (Year)	Duration of Intervention	Control Group (N randomized or enrolled)	Intervention Group(s) (N randomized or enrolled)	Fidelity
Piccirillo et al. (2013)[38]	4 weeks	**Sham rTMS (20)** 1-Hz-rTMS applied to left temporoparietal junction for all subjects with a stimulation intensity of 110%. Subjects received 5 sham stimuli sessions per week (1 per day) for 4 consecutive weeks. The sham magnet is identical in physical appearance to the active treatment magnet.	**rTMS (20)** 1-Hz-rTMS applied to left temporoparietal junction for all subjects with a stimulation intensity of 110%. Subjects received 5 stimuli sessions per week (1 per day) for 4 consecutive weeks.	Fourteen of 20 randomized patients completed study according to the protocol; 13 completed both treatment arms and 1 completed study arm 1 only.
Piccirillo et al. (2011)[39]	2 weeks	**Sham rTMS (14)** Neuronetics Model 2100 CRS with the sham coil designed to be identical in appearance and external design to the active treatment coil. The sham coil is modified so the magnetic flux is redirected away from the patient, back into the coil assembly. The sham coil was driven at a fixed level of 45% of the stimulator output. The patient received 5 stimulus sessions per week (1 per day) for 2 weeks.	**rTMS 1 Hz (14)** Active rTMS (1 Hz) with Neuronetics Model 2100, with a stimulation intensity of 110% or lower related to the individual resting motor threshold, to the left temporoparietal junction. The patient received 5 stimulus sessions per week (1 per day) for 2 weeks.weeks.	All patients completed both arms of treatment.
Plewnia et al. (2012)[33]	4 weeks	**Sham rTMS (16)** Magstim Super Rapid stimulator with a figure-eight coil; 3 pulses at 50 Hz given every 200 msec each working day for 4 weeks (20 sessions) with a stimulation intensity of 80% related to the individual resting motor threshold. Sham stimulation positioned behind the mastoid with the distance to the cortex precluding relevant cortex stimulation.	**Secondary auditory cortex rTMS (16)** Magstim Super Rapid stimulator with a figure-eight coil localized over the temporal cortex area (Brodmann area 42/22); 3 pulses at 50 Hz given every 200 msec each working day for 4 weeks (20 sessions) with a stimulation intensity of 80% related to the individual resting motor threshold. **Temporoparietal association cortex rTMS (16)** Magstim Super Rapid stimulator with a figure-eight coil localized over the temporoparietal cortex area (Brodmann area 39); 3 pulses at 50 Hz given every 200 msec each working day for 4 weeks (20 sessions) with a stimulation intensity of 80% related to the indiviudal resting motor threshold.	All but 8 patients completed all 20 sessions.
Plewnia et al. (2007)[40]	2 weeks	**Sham rTMS (6)** Magstim Rapid with coil placed at the lower occiput at the same distance to the ear allowing for the control stimulation to have similar noise and comparable aversive sensation to active rTMS.	**rTMS 1 Hz (6)** Magstim Rapid with 1 Hz rTMS applied to Brodmann area of the temporoparietal cortex with a stimulation intensity of 120% of the individual motor threshold. Stimulation received for 30 minutes, with 1,800 stimuli per session.	NR

Authors (Year)	Duration of Intervention	Control Group (N randomized or enrolled)	Intervention Group(s) (N randomized or enrolled)	Fidelity
Rossi et al. (2007)[41]	1 week	**Sham rTMS (16)** MagStim Super Rapid stimulator, 1,200 stimuli per daily session on 5 consecutive workdays with a stimulation intensity of 120% of motor threshold; placebo figure-of-eight coil positioned over the left temporoparietal region; the sham coil was titled to 90 degrees blocking the magnetic field from reaching cortical neurons at a biologically active level.	**rTMS 1 Hz (16)** Active rTMS (1 Hz) with MagStim Super Rapid stimulator, 1,200 stimuli per daily session on 5 consecutive workdays with a stimulation intensity of 120% of motor threshold; figure-of-eight coil positioned over the left temporoparietal region.	All but two patients completed treatment.
Sahlsten et al. (2017)[34]	10 days (over 2 weeks)	**Placebo rTMS (20)** Same as active rTMS except that a 15-cm plastic block was attached to the coil without the patient seeing it. The added distance effectively lowered the E field to the cortex to negligible amounts of 1–4 V/m.	**rTMS (22)** NBS System 4.0 (Nexstim, Ltd) to administer 4,000 pulses at a 1 Hz rate per daily session with 10 sessions applied over two weeks. Stimulation intensity at 100% of the resting motor threshold, figure-of-eight coil positioned over the left auditory cortex. Posterior regions of the auditory cortex chosen when tinnitus was high pitched and anterior regions of auditory cortex chosen when tinnitus low pitched.	All but 4 participants completed 10 full sessions. 1 participant in active rTMS had an abbreviated session due to late arrival. Two participants in placebo group received 8 sessions, and 1 participant received 6 full sessions.
Schecklmann et al. (2016)[35]	10 days (over 2 weeks)	**Sham cTBS (11)** Patients in the sham group received the same treatment as the active cTBS group, but the stimulation coil was titled away from the skull by 45 degrees over both wings.	**cTBS (12)** MagPro, MagOption, MC-B70 figure-of-eight coil with each burst consisting of three pulses, administered at a rate of 50 Hz over the left primary auditory cortex, with high frequency bursts continuously applied with an interstimulus interval of 200 milliseconds. Participants received a total of 1,200 pulses during a session.	NR
Vanneste et al. (2012)[42]	1 session	**Study 1 Sham rTMS (21)** Magstim Inc with a figure-eight coil placed over the left ventrolateral prefrontal cortex. Patients in the sham group received the same treatment as the active rTMS group, but the stimulation coil was placed perpendicular to the frontal area. Patients received 1 session total (200 pulses).	**Study 1 rTMS 1 Hz (21)** Magstim Inc with a figure-eight coil placed over the left ventrolateral prefrontal cortex. 1 -Hz-rTMS applied with a stimulation intensity of 80% of the motor threshold. Patients received 1 session total (200 pulses). **Study 2 Sham rTMS 10 Hz (39)** Magstim Inc with a figure-eight coil placed over the left ventrolateral prefrontal cortex. Patients in the sham group received the same treatment as the active rTMS group, but the stimulation coil was placed perpendicular to the	All completed the 1 session.

Authors (Year)	Duration of Intervention	Control Group (N randomized or enrolled)	Intervention Group(s) (N randomized or enrolled)	Fidelity
			frontal area. Patients rec **Study 2 rTMS 10 Hz(39)** Magstim Inc with a figure-eight coil placed over the left ventrolateral prefrontal cortex. 10 -Hz-rTMS applied with a stimulation intensity of 80% of the motor threshold. Patients received 1 session total (200 pulses).	
Vanneste et al. (2012)[43]	1 session	**Study 1 Sham rTMS (24)** Magstim Inc with a double-cone coil maximally tilted to the left intraparietal sulcus area. Patients in the sham group received the same treatment as the active rTMS groups, but the stimulation coil was placed perpendicular to the same area. Patient received 1 session (200 pulses).	**Study 1 rTMS 1-Hz (24)** Magstim Inc with a double-cone coil maximally tilted to the left intraparietal sulcus area. 1-Hz rTMS applied with a stimulation intensity of 80% of the motor threshold. Patient received 1 session (200 pulses). **Study 1 rTMS 10-Hz (24)** Magstim Inc with a double-cone coil maximally tilted to the left intraparietal sulcus area. 10-Hz rTMS applied with a stimulation intensity of 80% of the motor threshold. Patient received 1 session (200 pulses). **Study 2 Sham rTMS(40)** Magstim Inc with a double-cone coil placed symmetrically over the parietal cortex. Patients in the sham group received the same treatment as the active rTMS groups, but the stimulation coil was placed perpendicular to the same area. Patient received 1 session (200 pulses). **Study 2 rTMS 1-Hz(40)** Magstim Inc with a double-cone coil placed symmetrically over the parietal cortex. 1-Hz rTMS applied with a stimulation intensity of 80% of the motor threshold. Patient received 1 session (200 pulses). **Study 2 rTMS 5Hz(40)** Magstim Inc with a double-cone coil placed symmetrically over the parietal cortex. 5-Hz rTMS applied with a stimulation intensity of 80% of the motor threshold. Patient received 1 session (200 pulses). **Study 2 rTMS 10 Hz(40)** Magstim Inc with a double-cone coil placed symmetrically over the parietal cortex. 10-Hz rTMS applied with a stimulation intensity of 80% of the motor threshold. Patient received 1 session (200 pulses).	NR

Authors (Year)	Duration of Intervention	Control Group (N randomized or enrolled)	Intervention Group(s) (N randomized or enrolled)	Fidelity
Vanneste et al. (2011)[44]	1 session	**Sham rTMS (78)** Magstim Inc super rapid stimulator with a double-cone coil placed perpendicular to the frontal area at frequencies that yielded maximal tinnitus suppression rates; the stimulation session consisted of 200 pulses. The sham effect was performed after active rTMS procedures.	**rTMS 1 Hz (78)** Magstim Inc super rapid stimulator with a double-cone coil placed over the dorsal frontal cortex at a stimulation intensity fixed at 50% machine output for all patients; the stimulation session consisted of 200 pulses at 1 Hz. **rTMS 3 Hz (78)** Magstim Inc super rapid stimulator with a double-cone coil placed over the dorsal frontal cortex at a stimulation intensity fixed at 50% machine output for all patients; the stimulation session consisted of 200 pulses at 3 Hz. **rTMS 5 Hz(78)** Magstim Inc super rapid stimulator with a double-cone coil placed over the dorsal frontal cortex at a stimulation intensity fixed at 50% machine output for all patients; the stimulation session consisted of 200 pulses at 5 Hz. **rTMS 10 Hz(78)** Magstim Inc super rapid stimulator with a double-cone coil placed over the dorsal frontal cortex at a stimulation intensity fixed at 50% machine output for all patients; the stimulation session consisted of 200 pulses at 10 Hz. **rTMS 20 Hz(78)** Magstim Inc super rapid stimulator with a double-cone coil placed over the dorsal frontal cortex at a stimulation intensity fixed at 50% machine output for all patients; the stimulation session consisted of 200 pulses at 20 Hz.	NR

Abbreviations: cTBS = controlled theta-burst stimulation, a variation of rTMS; Hz = electromagnetic wavelength frequency; rTMS = repetitive transcranial magnetic stimulation.

Table D2d. Efficacy Outcomes for Included Repetitive Transcranial Magnetic Stimulation Interventions

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
Anders et al. (2010)[26] Sham rTMS (26) rTMS (26)	Tinnitus Handicap Inventory Yes	Mean change in score from baseline to week 2; N Sham: -3.4; 20; *P* = 0.05 rTMS: -5.3; 22; *P* = 0.01 Between-group difference: NR Mean change in score from baseline to 3.5-month followup; N Sham: -2.4; 20; *P* = 0.13 rTMS: -4.3; 22; *P* = 0.03 Between-group difference: NR Mean change in score from baseline to 6.5-month followup; N Sham: 1.2; 20; *P* = 0.29 rTMS: -3.8; 22; *P* = 0.06 Between-group difference: NR
	Tinnitus Questionnaire Yes	Mean change in score from baseline to 2-week followup; N Sham: -2.0; 20; *P* = 0.05 rTMS: -3.7; 22; *P* = 0.003 Between-group difference: NR Mean change in score from baseline to 3.5-month followup; N Sham: -0.8; 20; *P* = 0.27 rTMS: -3.5; 22; *P* = 0.02 Between-group difference: NR Mean change in score from baseline to 6.5-month followup; N Sham: 1.3; 20; *P* = 0.10 rTMS: -2.8; 22; *P* = 0.49 Between-group difference*: -4.0; NR
	VAS for severity Yes	Mean change in score from baseline to 2-week followup; N Sham: -2.2; 20; *P* = 0.24 rTMS: -4.3; 22; *P* = 0.07 Between-group difference: NR Mean change in score from baseline to 6.5--month followup; N Sham: 3.8; 20; *P* = 0.26 rTMS: -6.2; 22; *P* = 0.13 Between-group difference*: -10.0; NR
	VAS for	Mean change in score from baseline to 2-week followup; N

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
	disruption Yes	Sham: 0; 20; *P* = 0.21 rTMS: -0.9; 22; *P* = 0.28 Between-group difference: NR Mean change in score from baseline to 6.6-month followup; N Sham: 2.4; *P* = 0.33 rTMS: 0.3; *P* = 0.38 Between-group difference: NR
Barwood et al. (2013)[27] Sham rTMS (4) rTMS (4)	Tinnitus Handicap Inventory Yes	Median normalized gain score from baseline to week 1 onwards N = 8 Between-group difference: NR (active rTMS group reported lower handicap scores than sham group); *P*<0.05
Chung et al. (2012)[28] Sham rTMS (10) rTMS (12)	Tinnitus Handicap Inventory Yes	Mean (SD) change in score at 1-week followup; N Sham: 0 (4.2); 10 rTMS: -8.3 (7.9); 12 Between-group difference: -8.3*; *P*<0.01 Mean (SD) change in score at 1-month followup; N Sham: 0 (3.3); 10 rTMS: -5.3 (8.2); 12 Between-group difference: -5.3*; *P*>0.05
	Tinnitus Questionnaire Yes	Mean (SD) change in score at 1-week followup; N Sham: 0.1 (3.2); 10 rTMS: -8.6 (7.6); 12 Between-group difference: -8.7*; *P*<0.01 Mean (SD) change in score at 1-month followup; N Sham: 0.2 (2.6); 10 rTMS: -4.0 (6.4); 12 Between-group difference: -4.2*; *P*>0.05
Folmer et al. (2015)[29] Placebo rTMS (35) rTMS(35)	Tinnitus Functional Index Yes	Mean (SD) change in score after last treatment session; N Placebo: -1.8 (10.5); 32 rTMS: -5.2 (11.8); 32 Between-group difference*: -3.4 (95% CI, -9.0 to 2.2); *P* = 0.23 N (%) with decrease of >7 after last treatment session Placebo: 7 (22) rTMS: 18 (56) *P* = 0.005 RD* 34.4% (95% CI, 12.0% to 56.8%);

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
		RR* 2.6 (95% CI, 1.3 to 5.3) Mean (SD) change in score at 26 week; N Placebo: -2.9 (15.8); 32 rTMS: -13.8 (15.2); 32 Between-group difference*: -10.9 (95% CI, -18.6 to -3.2); *P* = 0.007 N (%) with decrease of >7 at 26 weeks Placebo: 12*(38) rTMS: 21*(66) *P* = 0.02 RD* 28.1% (95% CI, 4.6% to 51.6%); RR* 1.8 (95% CI, 1.05 to 2.9)
Formanek et al. (2018)[30] Sham rTMS (12) rTMS (20)	Tinnitus Handicap Inventory No	Mean (SD) change in score at 1-month followup; N Sham: -0.2 (8.0); 12 rTMS: -4.5 (11.7); 19 Between-group difference*: -4.3 (95% CI, -12.1 to 3.5); *P* = 0.27 Mean (SD) change in score at 6 months followup Sham: -4.3 (9.4); 12 rTMS: -9.1 (11.9); 20 Between-group difference*: -4.8 (95% CI, -13.0 to 3.4); *P* = 0.24 N (%) with improvement (undefined) at 1-month followup Sham:7*(58) rTMS: 13*(63) *P** = 0.80 RD* 4.7% (95% CI, -30.3% to 39.7%); RR* 1.08 (95% CI, 0.60 to 1.94) N (%) with improvement (undefined) at 6-month followup Sham: 8* (67) rTMS: 14* (70) *P** = 0.85 RD* 3.3% (95% CI, -30.1% to 36.7%) RR* 1.1 (0.64 to 1.7)
	Tinnitus Handicap Questionnaire No	Mean (SD) change in score at 1-month followup; N Sham: 1.1 (8.8) ; 12 rTMS: -1.5 (8.5); 19 Between-group difference*: -2.6 (95% CI, -9.0 to 3.8); *P* = 0.42

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
		Mean (SD) change in score at 6-month followup Sham: -2.8 (6.3); 12 rTMS: -6.1 (12.6); 20 Between-group difference*: -3.3 (95% CI, -11.3 to 4.7); *P* = 0.41 N (%) with improvement (undefined) at 1-month followup Sham: 6* (50) rTMS:13*(63) *P** = 0.50 RD* 13% (95% CI, -22.3% to 48.3%) RR* 1.3 (95% CI, 0.65 to 2.4) N (%) with improvement (undefined) at 6-month followup Sham:7*(58) rTMS: 13*(65) *P** = 0.72 RD* 6.7% (95% CI, -28.2 to 41.5) RR* 1.1 (95% CI, 0.62 to 2.0)
	Beck Depression Inventory No	Mean (SD) change in score at 1-month followup; N Sham: 0.6 (4.3); 12 rTMS: -0.5 (4.4); 19 Between-group difference*: -2.6 (95% CI, -9.1 to 3.9); *P* = 0.42 Mean (SD) change in score at 6 months followup Sham: 0.0 (3.6);12 rTMS: -0.1 (5.5); 20 Between-group difference*: -0.1 (95% CI, -3.7 to 3.5); *P* = 0.96 N (%) with improvement (undefined) at 1-month followup Sham: 4*(33) rTMS: 11*(53) *P** = 0.26 RD* 21.7% (95% CI, -12.8% to 56.1%) RR* 1.7 (95% CI, 0.68 to 4.0) N (%) with improvement (undefined) at 6-month followup Sham:5*(42) rTMS: 10*(50) *P** = 0.67 RD* 8.3% (95% CI, -27.1% to 43.8%)

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
		RR* 1.2 (95% CI, 0.54 to 2.7)
	Tinnitus Reaction Questionnaire No	Mean (SD) change in score at 1-month followup; N Sham: -1.5 (6.7); 12 rTMS: -4.9 (7.0); 19 Between-group difference*: -3.4 (95% CI, -8.6 to 1.8); *P* = 0.19 Mean (SD) change in score at 6 months followup Sham: -4.7 (8.2);12 rTMS: -9.1 (11.6); 20 Between-group difference*: -4.4 (95% CI, -12.2 to 3.4); *P* = 0.26 N (%) with improvement (undefined) at 1-month followup Sham: 7*(58) rTMS: 14*(68) *P** = 0.53 RD* 11.7%(95% CI, -22.7% to 46.0%) RR* 1.2 (95% CI, 0.69 to 2.1) N (%) with improvement (undefined) at 6-month followup Sham: 8*(67) rTMS: 14*(70) *P** = 0.85 RD* 3.3% (95% CI, -30.1% to 36.7%) RR* 1.1 (95% CI, 0.64 to 1.7)
Hoekstra et a. (2013)[31] Placebo (24) rTMS (26)	Tinnitus Handicap Inventory No	Mean change in score immediately after last treatment session Between-group differences: NR; *P* = 0.09 N (%) achieving at least 11 point (25%) reduction after the last treatment session Placebo: 3 (11.5) rTMS: 6 (23.1) *P* = 0.47 RD* 10.6% (95% CI, -19.3% to 31.5%) RR* 1.8 (95% CI, 0.52 to 6.6) Mean change in score at 3 months Between-group differences: NR; *P* = 0.42 Mean change in score at 6 months Between-group differences: NR; *P* = 0.06
	Tinnitus Questionnaire	Mean change in score immediately after last treatment session Between-group differences: NR; *P* = 0.80

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
	Yes	N (%) with decrease of > = 10 immediately after last treatment session Placebo: 4 (16.7*) rTMS: 3 (11.5*) *P** = 0.63 RD* -5.1% (95% CI, -24.4% to 14.2%); RR* 0.69 (95% CI, 0.17 to 2.8) Mean change in score at 3 months Between-group differences: NR; *P* = 0.82 Mean change in score at 6 months Between-group differences: NR; *P* = .32
	VAS for distress No	Mean change score immediately after last treatment session Between-group differences: NR; *P* = 38 Mean change in score at 3 months Between-group differences: NR; *P* = 32 Mean change in score at 6 months Between-group differences: NR; *P* = 77
Kleinjung et al. (2005)[36] Langguth et al. (2007)[191]	Tinnitus Questionnaire Yes	Mean (SD) change in score at 11-day followup; N Sham rTMS*: -0.6 (4.2); 10 rTMS*: -3.7 (3.8); 10 Between-group difference*: -3.1 (95% CI, -6.9 to .66); *P* = 0.10
Landgrebe et al. (2017)[32] Sham rTMS (75) rTMS (71)	Tinnitus Questionnaire Yes	Mean (SD) change in score at day 12 Between-group difference: -1.0 (95% CI, -3.2 to 1.2); *P* = .36 Mean change in score from baseline to week 26 Between-group difference: NR; *P* = 0.53
	Tinnitus Handicap Inventory No	Mean change in scale scores from baseline to week 26 Between-group differences: NR;: *P*>0.11
	Beck Depression Inventory No	Mean change in score from baseline to day 12 Between-group difference: -0.5 (95% CI, -1.6 to 0.7); *P* = 0.43 Mean change in score from baseline to week 26 Between-group difference: NR; *P* = 0.78
	Clinical Global Impression of Change No	Mean change in score from baseline to week 26 Between-group differences: NR: *P* = 0.12

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
	Tinnitus Severity Scales No	Mean change from baseline to 26 weeks Between-group differences: NR, *P*>0.11
	SF-12 Physical Health Component Score No	Mean change in score from baseline to week 26 Between-group difference: NR; *P* = 0.14
	SF-12 Mental Health Component Score No	Mean change in score from baseline to week 26 Between-group difference: NR; *P* = 0.14
Mennemeier et al. (2011)[37] Sham rTMS (21) rTMS 1 Hz (21)	NR	NR
Piccirillo et la. (2013)[38] Sham rTMS (20) rTMS (20)	Tinnitus Handicap Inventory Yes	Median difference in THI score between the change associated with active and sham at 4 weeks N = 14 Between-group difference: 4 (95% CI, -9 to 10); *P*>0.05
Piccirillo et al. (2011)[39] Sham rTMS (14) rTMS 1 Hz (14)	Tinnitus Handicap Inventory Yes	Median (95% CI) change in score immediately after; N Sham: 6 (-2 to 12); 14 rTMS 1 Hz: 5 (0 to 14); 14 Between-group difference: 1 (95% CI, -6 to 4); NR
	Patient global impression of change	N (%) with poor response immediately after Sham: 11 (79) rTMS: 12 (86) *P** = 0.66 RD* 7.1% (95% CI, -21.1% to 35.4%); RR* 1.09 (95% CI, 0.77 to 1.5) N (%) with fair response immediately after Sham: 2 (14) rTMS: 2 (14) *P**>0.99 RD* 0% (95% CI, -25.9% to 25.9%);

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
		RR* 1.0 (95% CI, 0.16 to 6.1) N (%) with good response immediately after Sham: 1 (7) rTMS: 0 (0) *P** = 0.5 RD* -7.14% (95% CI, -20.6% to 6.3%);
	Body Symptom Index No	Median change in score (95% CI) immediately after; N Sham: 1.5*; 14 rTMS: 1.5*; 14 Between-group difference: 0; *P*>0.05
	Beck Depression Inventory No	Median change in score immediately after; N Sham: 3*; 14 rTMS: 3.5*; 14 Between-group difference: 0.5; *P*>0.05
Plewnia et la. (2012)[33] Sham rTMS (16) Secondary auditory cortex rTMS (16) Temporoparietal association cortex rTMS (16)	Tinnitus Questionnaire Yes	Mean (SE) change in score at 4-week followup; N Secondary auditory cortex rTMS vs. sham rTMS Between-group difference: -0.1 (95% CI, -5.1 to 5.0) Tempoparietal association cortex rTMS vs. sham rTMS Between-group difference: 0.6 (95% CI, -4.5 to 5.6) Mean (SE) change in score at 3 months followup; N Sham rTMS: 0.3 (1.6); 16 Secondary auditory cortex rTMS: -3.1 (4.1); 16 Tempoparietal association cortex rTMS: -1.4 (1.5); 16 Secondary auditory cortex rTMS vs. sham rTMS Between-group difference: -3.4*; *P* NS Tempoparietal association cortex rTMS vs. sham rTMS Between-group difference: -1.7*; *P* NS
	Global change No	Global tinnitus change (6 point scale) at 4 weeks followup; N = 32 Secondary auditory cortex rTMS vs. sham rTMS OR 1.5 (95% CI, .28 to 9.3) Tempoparietal association cortex rTMS vs. sham rTMS OR 2.0 (95% CI, 0.50 to 9.0)
Plewnia et la. (2007)[40] Sham rTMS (6) rTMS 1 Hz (6)	Tinnitus Questionnaire Yes	Mean Percentage Difference (SD) in TQ between sham and rTMS immediately after treatment: -19.4%* (16.6%)* *P* = 0.022 All scores returned to baseline values 2 weeks after treatment

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
	VAS for tinnitus loudness No	Median change in score at immediate followup; N Sham: -0.5 rTMS: -1 Between-group difference: -0.5*
	VAS for tinnitus annoyance No	Median change in score at immediate followup Sham: -0.5 rTMS: -1 Between-group difference: -0.5*
Rossi et el. (2007)[41] Sham rTMS (16) rTMS 1 Hz (16)	VAS for tinnitus discomfort Yes	Mean change in score from baseline to immediately after; N Sham: -.66*; 14; *P* = 0.43 rTMS 1 Hz: -1.97*; 14; *P* = 0.03 Between-group difference: -1.31*; 14; *P* = 0.02 Mean change in score from baseline to week 1; N Sham: -.62*; 14; *P* = 0.49 rTMS 1 Hz: -1.5*; 14; *P* = 0.03 Between-group difference: -.88*; 14; *P* = 0.02 Mean change in score from baseline to week 2; N Sham: -.62*; 14; *P* = 0.49 rTMS 1 Hz: -.29*; 14; *P* = 0.71 Between-group difference: .33*; 14; *P* = 0.60
	Hamilton Depression Rating Scale NR	Mean change in score from baseline to immediately after Sham: -0.5*; *P* = 0.25 rTMS 1 Hz: -1.2*; *P* = 0.13 Between-group difference: -0.7*; *P* NR but likely NS Mean change in score from baseline to week 1 Sham: -0.5*; *P* = 0.25 rTMS 1 Hz: -1.2*; *P* = 0.125 Between-group difference: -0.7*; *P* NR but likely NS Mean change in score from baseline to week 2 Sham: -0.5*; *P* = 0.25 rTMS 1 Hz: -0.3*; *P* = 0.5 Between-group difference: 0.2*; *P* NR but likely NS
	Hamilton Anxiety Rating Scale NR	Mean change in score from baseline to immediately after Sham: -0.2*; *P* = 0.06 rTMS 1 Hz: -0.7*; *P* = 0.94

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
		Between-group difference: -0.5*; *P* NR but likely NS Mean change in score from baseline to week 1 Sham: -0.2*; *P* = 0.84 rTMS 1 Hz: -0.7*; *P* = 0.09 Between-group difference: -0.5*; *P* NR but likely NS Mean change in score from baseline to week 2 Sham: -0.2*; *P* = 0.94 rTMS 1 Hz: -0.2*; *P* = 0.69 Between-group difference: 0*; *P* NR but likely NS
Sahlsten et al. (2017)[34] Placebo rTMS (20) rTMS (22)	Tinnitus Handicap Inventory Yes	Median change in score at 6 months Between-group difference: NR; *P* = 0.28 N (%) of participants with THI reduction > = 6 immediately following treatment completion Placebo: 13 (65) rTMS: 11 (58) *P* = 0.75 RD* -7.1% (-37.6% to 23.4%) RR* .89 (95% CI, 0.54 to 1.5) N(%) of participants with THI reduction > = 6 at 3 months Placebo: 12 (60) rTMS: 13 (68) *P* = 0.74 RD* 1.8% (95% CI, -28.3% to 32.0%) RR* 1.03 (95% CI, 0.64 to 1.6) N(%) of participants with THI reduction > = 6 at 6 months Placebo: 14 (70) rTMS: 15 (79) *P* = 0.72 RD* 9.0% (95% CI, -18.2% to 36.1%); RR* 1.1 (95% CI, 0.78 to 1.6)
	VAS for tinnitus annoyance Yes	Median change in score over 3 months Between-group difference: NR; *P* = 0.82
	VAS for tinnitus loudness Yes	Median change in score over 3 months Between-group difference: NR; *P* = 0.50 N(%) of participants with reduction > = 30% immediately following treatment completion

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
		Placebo: 6 (30) rTMS: 10 (53) *P* = 0.20 RD* 22.6% (95% CI, -7.5% to 52.8%); RR* 1.8 (95% CI, 0.79 to 3.9) N(%) of participants with reduction > = 30% at 3m Placebo: 7 (35) rTMS: 9 (47) *P* = 0.52 RD* 12.4% (95% CI, -18.3% to 43.0%); RR* 1.4 (95% CI, 0.63, to 2.9)
	VAS for distress Yes	Median change in score over 3 months Between-group difference: NR; *P* = 0.46
	Beck Depression Inventory No	Median change in score over 3 months Between-group differences: NR; *P* = 0.52
	Jenkins Sleep Questionnaire No	Median change in score over 3 months Between-group difference: NR, *P* = 0.63
Schecklmann et al. (2016)[35] Sham cTBS (11) cTBS (12)	Tinnitus Handicap Inventory No	Mean change in score at week 8 Between-group difference: NR; *P*>0.12
	Tinnitus Questionnaire No	Mean change in score at week 8 Between-group difference: NR; *P*>0.12
	VAS for tinnitus loudness No	Mean change in score at week 8 Between-group difference: NR; *P*>0.12
	VAS for tinnitus annoyance No	Mean change in score at week 8 Between-group difference: NR; *P*>0.12
	VAS for discomfort, ignorability, unpleasantness	Mean change in score at week 8 Between-group difference: NR; *P*>0.12

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
	No	
Vanneste et al. (2012)[42] Study 1 Sham rTMS (21) Study 1 rTMS 1 Hz (21) Study 2 Sham rTMS 10 Hz (39) Study 2 rTMS 10 Hz (39)	VAS for tinnitus loudness Yes	1-Hz vs. Sham Mean (SD) change in score at unreported time point; N Sham: -0.6* (NR); 21 rTMS: -0.2* (NR); 21 Between-group difference*: 0.4; Not explicitly reported but appears to be NS 10-Hz rTMS vs. Sham Mean (SD) change in score at unreported time point; N Sham: -0.3* (NR); 39 rTMS: -1.8* (NR); 39 Between-group difference*: -1.4; *P*<0.001
Vanneste et al. (2012)[43] Study 1 Sham rTMS (24) Study 1 rTMS 1-Hz (24) Study 1 rTMS 10-Hz (24) Study 2 Sham rTMS (40 Study 2 rTMS 1-Hz (40 Study 2 rTMS 5Hz (40) Study 2 rTMS 10 Hz (40)	VAS for tinnitus loudness Yes	Study 1: 1-Hz vs. Sham Mean (SD) change in score at unreported time point; N Sham: 0.0* (NR); 24 rTMS: -0.1* (NR); 24 Between-group difference*: 0.0; NR Study 1: 10-Hz vs. Sham Mean (SD) change in score at unreported time point; N Sham: 0.0* (NR); 24 rTMS: -0.9* (NR); 24 Between-group difference*: -0.8; NR Study 2: 1-Hz vs. Sham Mean (SD) change in score at unreported time point; N Sham: -0.6* (NR); 40 rTMS: -0.7* (NR); 40 Between-group difference*: -0.1; NR Study 2: 5-Hz vs. Sham Mean (SD) change in score at unreported time point; N Sham: -0.6* (NR); 40 rTMS: -1.1* (NR); 40 Between-group difference*: -0.5; NR Study 2: 10-Hz vs. Sham Mean (SD) change in score at unreported time point; N Sham: -0.6* (NR); 40 rTMS: -1.1* (NR); 40

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
		Between-group difference*: -0.5; NR
Vanneste et al. (2011)[44] Sham rTMS (78) rTMS 1 Hz (78) rTMS 3 Hz (78) rTMS 5 Hz (78 rTMS 10 Hz (78 rTMS 20 Hz (78)	VAS for tinnitus loudness Yes	Amount of suppression (% reduction) in score at NR followup Sham: 3.5 rTMS 1 Hz: 10.8 1 Hz vs. sham between-group difference: 7.3*; *P*<0.05 favoring rTMS rTMS 3 Hz: 10.2 3 Hz vs. sham between-group difference: 6.7*; *P*<0.05 favoring rTMS rTMS 5 Hz: 5.6 5 Hz vs. sham between-group difference: 2.1*; *P* NS rTMS 10 Hz: 6.2 10 Hz vs. sham between-group difference: 2.7*; *P* NS rTMS 20 Hz: .45 20 Hz vs. sham between-group difference: -3.1*; *P*<0.05 favoring sham
	VAS for distress Yes	Amount of suppression (% reduction) in score at NR followup Sham: 3.5 rTMS 1 Hz: 11.7 1 Hz vs. sham between-group difference: 8.2*; *P*<0.05 favoring rTMS rTMS 3 Hz: 11.7 3 Hz vs. sham between-group difference: 8.2*; *P*<0.05 favoring rTMS rTMS 5 Hz: 1.5 5 Hz vs. sham between-group difference: -2.0*; *P* NS rTMS 10 Hz: .25 10 Hz vs. sham between-group difference: -3.3*; *P*<0.05 favoring sham rTMS 20 Hz: .45 20 Hz vs. sham between-group difference: -3.1*; *P*<0.05 favoring sham

Notes: * Indicates a data value that we calculated based on data provided in the publication.

Abbreviations: Hz = electromagnetic wave frequency; NR = not reported; NS = not significant; RD: risk difference; RR: Risk ratio. rTMS = repetitive transcranial magnetic stimulation; SE: standard error; SD = standard deviation; TFI = Tinnitus Functional Index; THI = Tinnitus Handicap Inventory; TQ = Tinnitus Questionnaire; VAS = visual analog scale.

Table D2e. Safety and Cost Outcomes for Included Repetitive Transcranial Magnetic Stimulation Interventions

Authors (Year) Interventions (N Randomized)	Safety Outcomes	Cost Outcomes
Anders et al. (2010)[26] Sham rTMS (26) rTMS (26)	Sham: 2 patients withdrew due to headache rTMS: 2 patients withdrew due to worsening of tinnitus, 1 patient withdrew due to headache, and 1 patient withdrew due to pain at the site of stimulation. Among those in the sham treated group who completed all treatment sessions: mild headache, transient worsening of tinnitus, and changes in the quality of sleep were reported. Among those in the rTMS group who completed all treatment sessions: headache, mild tongue paresthesia, transient worsening of tinnitus, and changes in quality of sleep were reported. Zero patients developed seizures or other serious side effects.	NR
Barwood et al. (2013)[27] Sham rTMS (4)	NR	NR
Chung et al. (2012)[28] Sham rTMS (10) rTMS (12)	No patient experienced sustained side effects after the rTMS treatment. 5 patients reported transient jaw soreness, 3 patients developed temporary orbital twitching, and 1 patient experienced facial myalgia during stimulation.	NR
Folmer et al. (2015)[29] Placebo rTMS (35) rTMS (35)	No participants withdrew because of adverse effects of rTMS	NR
Formanek et al. (2018)[30] Sham rTMS (12) rTMS (20)	N (%) with side effects Sham: 3 (25*) [headache, dizziness, blurred vision] rTMS: 3 (15*) [all headache]	NR
Hoekstra et al. (2013)[31] Placebo (24) rTMS (26)	N(%) with side effects Placebo: 1 (3.9) headache rTMS: 5 (19.2) All 5 experienced headaches, 1 experienced additional dizziness and 1 additionally experienced a sensation of 'licking a battery.'	NR
Kleinjung et al. (2005)[36] Langguth et al. (2007)[191] Sham rTMS (10) rTMS (10)	"Adverse effects were not observed."	NR
Landgrebe et al. (2017)[32] Sham rTMS (75) rTMS (71)	N (%) with AE Sham: 30* (39.5) rTMS: 26*(35.1) ARD -4.3% (95% CI, -19.3% to 10.9%) The majority of AEs were mild to moderate severity. N (%) with SAE Sham: 1 (1.3*) [severe headache and deterioration of the tinnitus] rTMS: 1 (1.4*) [tachyarrhythmia in context of a known cardiac insufficiency]	NR

Authors (Year) Interventions (N Randomized)	Safety Outcomes	Cost Outcomes
	In both groups, headache was the most frequently reported AE (sham 14.5% vs. rTMS 10.8%)	
Mennemeier et al. (2011)[37] Sham rTMS (21) rTMS 1 Hz (21)	No detrimental effects of active or sham rTMS observed on any of the neuropsychological tests and there were no reported changes in hearing at the end of treatment.	NR
Piccirillo et al. (2013)[38] Sham rTMS (20) rTMS (20)	There were no serious adverse effects (related or non-related), The most common adverse event was jaw twitch. Other minimal adverse effects included headache, worsening of tinnitus, increased sensitivity to noise, painful local sensation, and sleep disturbance.	NR
Piccirillo et al. (2011)[39] Sham rTMS (14) rTMS 1 Hz (14)	No serious adverse events reported. The most common AEs included jaw twitch (mild in 5 and moderate in 1) and neck or shoulder tightness or twitch (mild in 4 and severe in 1). The number of AEs reported was greater (but not significant) during the active treatment (11 events) compared with sham treatment (8 events) (P = 0.42).	NA
Plewnia et al. (2012)[33] Sham rTMS (16) Secondary auditory cortex rTMS (16) Temporoparietal association cortex rTMS et al. (16)	Headache Sham rTMS: 3 Secondary Auditory Cortex rTMS: 2 Tempoparietal association cortex rTMS: 2 Worsening of tinnitus Sham rTMS: 3 Secondary Auditory Cortex rTMS: 1 Tempoparietal association cortex rTMS: 2 Increased sensitivity to noise Sham rTMS: 1 Secondary Auditory Cortex rTMS: 0 Tempoparietal association cortex rTMS: 1 Painful local sensation Sham rTMS: 0 Secondary Auditory Cortex rTMS: 1 Tempoparietal association cortex rTMS: 0 Sleep disturbance Sham rTMS: 0 Secondary Auditory Cortex rTMS:1 Tempoparietal association cortex rTMS: 0	NR
Plewnia et al. (2007)[40] Sham rTMS (6) rTMS 1 Hz (6)	No side effects of stimulation were observed or reported by patients.	NR
Rossi et al. (2007)[41] Sham rTMS (16) rTMS 1 Hz (16)	Patients (number NR) reported slight transient headache on the stimulation site during rTMS. Approximately 30% of patients complained of tongue paraesthesia during active rTMS. Majority of patients did not report side effects from rTMS.	NR

Authors (Year) Interventions (N Randomized)	Safety Outcomes	Cost Outcomes
Sahlsten et al. (2017)[34] Placebo rTMS (20) rTMS (22)	There were no major side effects. Some patients reported local irritation due to muscle twitching at the stimulation side and mild temporary side effects such as headaches; actual numbers of participants experiencing side effects was NR.	NR
Schecklmann et al. (2016)[35] Sham cTBS (11) cTBS (12)	NR	NR
Vanneste et al. (2012)[42] Study 1 Sham rTMS (21) Study 1 rTMS 1 Hz (21) Study 2 Sham rTMS 10 Hz (39) Study 2 rTMS 10 Hz (39)	NR	NR
Vanneste et al. (2012)[43] Study 1 Sham rTMS (24) Study 1 rTMS 1-Hz (24) Study 1 rTMS 10-Hz (24) Study 2 Sham rTMS (40 Study 2 rTMS 1-Hz (40 Study 2 rTMS 5Hz (40) Study 2 rTMS 10 Hz (40)	NR	NR
Vanneste et al. (2011)[44] Sham rTMS (78) rTMS 1 Hz (78) rTMS 3 Hz (78) rTMS 5 Hz (78 rTMS 10 Hz (78 rTMS 20 Hz (78)	NR	NR

Table D3a. Study Characteristics For Included Cognitive Behavioral Interventions

Authors (Year)	Study Design	Sponsor	Country	Eligible Study Arms	Total N Overall/ Total N in Eligible Study Arms	Risk of Bias
Abbott et al. (2009)[64]	Cluster RCT	Australian Research Council and BP Australia	Australia	Information-only control (24) Internet-based CBT (32)	56/ 56	High
Andersson et al. (2005)[57]	RCT	Swedish Hard of Hearing Association	Sweden	Waitlist control (11) Internet-based CBT (12)	23/ 23	High
Andersson et al. (2002)[60]	RCT	Swedish Council for Social Research and the Swedish Hard of Hearing Association	Sweden	Waitlist control (64) Group-based CBT (53)	117/ 117	High
Beukes et al. (2018)[46] Beukes et al. (2018)[192]	RCT	This article presents independent research not from any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.	U.K.	Attention-only control (73) Internet-based CBT (73)	146/ 146	Some concerns
Henry et al. (2018)[45]	RCT	VA Rehabilitation Research and Development Service	U.S.	Waitlist control (104) Individual, telephone-based CBT (101)	205/ 205	Some concerns
Henry et al. (2017)[47]	RCT	VA Rehabilitation Research & Development Service	U.S.	Waitlist control (150) Group-based CBT (150)	300/ 300	High
Henry et al. (1998)[63]	RCT	NR	Australia	Waitlist control (12) Group-based CBT (12)	54/ 24	High
Henry et al. (1996)[62]	RCT	NR	Australia	Waitlist control (20) Group-based CBT (20)	63/ 60	High
Hesser et al. (2012)[51]	RCT	Swedish Council for Working Life and Social Research	Sweden	Online discussion forum control (32) Internet-based CBT (32)	99/ 64	Some concerns
Jasper et al.(2014)[49] Conrad et al. (2015)[193]	RCT	Swedish Research Council	Germany	Online discussion forum control (44) Group-based CBT (43) Internet-based CBT (41)	128/ 128	Some concerns
Kaldo et al. (2007)[55]	RCT	Swedish Hard of Hearing Association	Sweden	Waitlist control (38) Book-guided CBT (34)	72/ 72	Some concerns
Kroner-Herwig et al. (2003)[59]	RCT	German Ministry of Research and Technology	Germany	Waitlist control (20) Group-based CBT (43)	76/ 116	High
Malouff et al. (2010)[52]	RCT	American Tinnitus Association	Australia	Waitlist control (78) Book-guided CBT (84)	162/ 162	High

Authors (Year)	Study Design	Sponsor	Country	Eligible Study Arms	Total N Overall/ Total N in Eligible Study Arms	Risk of Bias
Martz et al. (2018)[61]	RCT	VA Rehabilitation Research and Development Service	U.S.	Waitlist control (10) Group-based CBT (10)	40/ 20	High
Nyenhuis et al. (2013)[50]	RCT	German Federal Ministry of Research and Education	Germany	Information-only control (77) Book-guided CBT (77) Internet-based CBT (79) Group-based CBT (71)	304/ 304	Some concerns
Robinson et al. (2008)[53]	RCT	American Tinnitus Association and NIH	U.S.	Waitlist control (27) Group-based CBT (38)	65/ 65	High
Sadlier et al. (2008)[56]	Controlled Trial	NR	U.K.	Waitlist control (11) Individual-based CBT (14)	25/ 25	High
Weise et al. (2016)[48]	RCT	Swedish Research Council	Germany	Online discussion forum control (62) Internet-based CBT (62)	124/ 124	Some concerns
Weise et al. (2008)[54]	RCT	German Research Foundation	Germany	Waitlist control (67) Individual-based CBT (63)	130/ 130	Some concerns
Zachriat et al. (2004)[58]	RCT	Geers Foundation grant, noise generators donated by Hansaton, batteries donated by Energizer, sound generators fitted by Reuters Acoustics	Germany	Education-only control (23) Group-based CBT (29) Tinnitus retraining therapy (31)	77/ 77	High
Zenner et al. (2013)[65]	Controlled clinical trial	Ministry of Research and Technology (BMFT) in Germany and Mediceon	Germany	Waitlist control (120) Individual-based CBT (166)	286/ 286	High

Abbreviations: CBT = cognitive behavioral therapy; RCT = randomized controlled trial; U.K. = United Kingdom; U.S. = United States.

Table D3b. Population Characteristics for Included Cognitive Behavioral Therapy Interventions

Authors (Year)	Study Population	Mean Age (SD)	N (%) Female	N (%) Race/Ethnicity	Other Characteristics
Abbott et al. (2009)[64]	Adults with tinnitus recruited from 23 different worksites. *Inclusion:* Age 18 to 65, tinnitus for at least 3 months and diagnosed by a clinician, access to the internet. *Exclusion:* Receiving current psychological treatment for tinnitus.	Control: 48.7 (8.6) CBT: 50.5 (9.5)	5 (10*)	NR	*Tinnitus Duration* Mean (SD) tinnitus duration in months Control: 60.3 (53.8) CBT: 140.2 (115.3) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled
Andersson et al. (2005)[57]	Adults with sufficiently bothersome tinnitus for at least 6 months recruited through advertisements. *Inclusion:* Bothersome tinnitus, tinnitus for at least 6 months, ability to walk up stairs to therapy room. *Exclusion:* Previous psychological treatment for tinnitus, BDI score > 22, BDI score >2 on hopelessness or suicidal ideation items, medical reasons for not participating in treatment.	70.1 (3.9)	11 (47.8*)	NR	*Tinnitus Duration* Mean (SD) in years 13 (12.5) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled
Andersson et al. (2002)[60]	Adults with tinnitus recruited by newspaper ads and posts on the Swedish Hard of Hearing Association webpage. *Inclusion:* Age 18 to 70 hears, tinnitus for at least 6 months, saw a general practitioner or ENT practitioner for tinnitus. *Exclusion:* Tinnitus not a severe problem.	Control: 47.2 (15.0) CBT: 48.5 (12.3)	Control: 31*(48) CBT: 24*(46)	NR	*Tinnitus Duration* Mean (SD) duration in years Control: 6.4 (6.8) CBT: 6.2 (5.6) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled
Beukes et al. (2018)[46] Beukes et al. (2018)[192]	Adult men and women with "significant levels of tinnitus distress." *Inclusion:* Adults 18 years and older who have had tinnitus for at least 3 months, had a score of 25 or more on the Tinnitus Functional Index, who lived in the U.K., and had internet access. *Exclusion:* Anyone with objective or unilateral tinnitus, suffered tinnitus due to a medical disorder, were concurrently receiving tinnitus treatment, or reported any major medical,	55.6 (12.9)	63 (43)	NR	*Tinnitus Duration* 11.7 (11.9), Range (0.3–56) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled *Other* N (%) using hearing aids: 54 (37)

Authors (Year)	Study Population	Mean Age (SD)	N (%) Female	N (%) Race/Ethnicity	Other Characteristics
	psychiatric, or mental disorder.				
Henry et al. (2018)[45]	Adults throughout the U.S. including civilians yet with special efforts made to enroll Veterans and Military Service Members with a history of traumatic brain injury. *Inclusion:* Adults with clinically significant tinnitus as indicated by the Tinnitus Hearing Survey (THS), a hearing test within previous two years, hearing aids if recommended at the time of most recent hearing test with at least 1 month of wear to fully acclimate to them, capable of participating by telephone. *Exclusion:* Active suicidal ideation.	59.0 (10.5)	30 (14)	American Indian or Alaska Native: 2 (1) Asian or Pacific Islander: 3 (1) Black: 28 (14) Hispanic: 3 (1) White: 159 (78) Other: 8 (4) Prefer not to answer: 2 (1)	*Tinnitus Duration* NR *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled *Other* N (%) Veteran: 174 (85) N (%) with mild TBI: 44 (21) N (%) with moderate to severe TBI: 18 (8)
Henry et al. (2017)[47]	Adults with tinnitus symptoms for less than one year recruited from 2 Veterans Administration Medical Center audiology clinics. *Inclusion:* Identification of at least one current tinnitus-specific problem per the Tinnitus and Hearing Survey, willing to attend coping skills workshops. *Exclusion:* NR	58(13)# #For N = 297 (no baseline data on 3 participants that were randomized)	15* (5)	American Indian/Alaska native: 9* (3) Black: 80* (27) Hispanic: 9* (3) White: 196* (66) Other: 3* (1)	*Tinnitus Duration* <1 y: 12* (4) 1 to 2 y: 24* (8) 3 to 5 y: 30* (10) 6 to 10 y: 24* (8) 11 to 20 y: 33* (11) > 20 y: 131* (44) Unsure: 45* (15) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled
Henry et al. (1998)[63]	Adults with tinnitus for more than 6 months recruited from radio and newspaper advertisements. *Inclusion:* Primary complaint of tinnitus for more than 6 months, prior assessment by an otaryngologist and an audiologist, traditional treatments not recommended or failed, TRQ > = 17 points. *Exclusion:* NR	56.3 (NR)#	19 (38*)#	NR	*Tinnitus Duration* NR *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled
Henry et al. (1996)[62]	Adults with tinnitus for more than 6 months referred by audiologists and otolaryngologists at a Veteran's Hospital outpatient clinic. *Inclusion:* Primary complaint of tinnitus for more than 6 months; assessment by an	64.6 (NR)	8 (13*)	NR	*Tinnitus Duration* NR *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled

Authors (Year)	Study Population	Mean Age (SD)	N (%) Female	N (%) Race/Ethnicity	Other Characteristics
	otaryngologist and an audiologist; traditional treatments were not recommended or tried and failed; had not been provided a hearing aid, masker, or medication in the previous 6 months; TRQ > 17. *Exclusion:* NR				
Hesser et al. (2012)[51]	Adults with moderate to severe tinnitus recruited through media and internet advertisements. *Inclusion:* Tinnitus for more than 6 months, diagnosis confirmed by ENT practitioner, moderate to severe distress from tinnitus *Exclusion:* Severe medical or psychiatric condition, imminent suicide risk, ongoing treatment for tinnitus, or had previously received the treatments that were offered in study.	48.5 (14.7)	43 (43.4)	NR	*Tinnitus Duration* Mean (SD) in months: 9.2 (8.3) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled
Jasper et al. (2014)[49] Conrad et al. (2015)[193]	Adult with chronic tinnitus recruited through 1) an outpatient clinic, 2) German Tinnitus Association, 3) referrals from otolaryngologists, and 4) newspaper advertisements and flyers. *Inclusion:* Adults 18 years or older who had tinnitus for at least 6 months and scored 18 and above on the THI, or 8 and above on the Mini-TQ. Participants had to have been examined by an otolaryngologists, have internet access, and the ability to attend weekly group sessions. *Exclusion:* Concurrent psychological treatment for tinnitus, tinnitus caused by a medical condition or otologic disease (e.g., active Meniere's Disease), or major medical or psychiatric condition.	Control: 52.1 (9.0) Group CBT: 50.2 (13.1) Internet CBT: 51.3 (9.8)	Control: 16 (36.4) Group CBT: 19 (44.2) Internet CBT: 16 (39.0)	NR	*Tinnitus Duration* Mean (SD) duration in months Control: 95.4 (84.9) Group CBT: 100.2 (82.2) Internet CBT: 110.9 (94.6) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled
Kaldo et al. (2007)[55]	Adults 18 years of age or older with distressing tinnitus for at least 6 months recruited by newspaper and Internet advertisements and articles and waiting lists at	Control: 48.5 (15.7) CBT: 45.9 (13)	Control: 18 (47) CBT: 17 (50)	NR	*Tinnitus Duration* Mean (SD) in years Control: 12.4 (11.7) CBT: 8.6 (8.4)

Authors (Year)	Study Population	Mean Age (SD)	N (%) Female	N (%) Race/Ethnicity	Other Characteristics
	a university hospital audiology department *Inclusion:* Exam by ENT practitioner or audiologist, tinnitus for at least 6 months, available to complete intervention, TRQ score > = 10, HADS score < = 18 for anxiety and depression subscales *Exclusion:* Comorbid conditions requiring immediate medical treatment				*Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled
Kroner-Herwig et al. (2003)[59]	Adults with idiopathic tinnitus for more than 6 months recruited by newspaper announcements. *Inclusion:* Age 18 to 65 years, reported tinnitus was main health problem, tinnitus for more than 6 months, tinnitus determined to be idiopathic in nature, average VAS rating (0-100) > = 40 on 9 subjective annoyance tinnitus scales. *Exclusion:* Hearing loss severe enough to prevent group participation, Meniere disease, currently in psychotherapeutic treatment.	Control: 47.3 (7.9) CBT: 44.7 (12.7)	Control: 10*(50) CBT: 24*(55.8)	NR	*Tinnitus Duration* Mean (SD) duration of tinnitus in months Control: 57.4 (44.9) CBT: 55.4 (51.5) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled
Malouff et al. (2010)[52]	Adults with tinnitus recruited through postings on tinnitus support Web pages, announcements at in-person tinnitus support groups, postings in audiology practices, and media releases. *Inclusion:* Adults with self-reported tinnitus as assessed by items on the Tinnitus Severity Scale. *Exclusion:* No exclusion criteria	Control: 57.8 (13.3) CBT: 57.3 (13.7)	72* (44*)	NR	*Tinnitus Duration* NR *Hearing Loss* Hearing loss was not required or excluded, and no mention of this characteristic was made in describing the study population
Martz et al. (2018)[61]	Adults with tinnitus and a score of at least 21 on the TFI recruited by internet and newspaper ads and flyers at VA sites *Inclusion:* Score > = 21 on TFI, 2 errors or less on 6-item cognitive screening instrument, use hearing aids if needed. *Exclusion:* Previous participation in progressive tinnitus management program or focus groups used to develop training	57.8 (16.4)#	8 (20)#	White: 37*(92.3)# African American: 1*(2.5)# Hispanic: 1*(2.5)# Other: 1*(2.5)#	*Tinnitus Duration* NR *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled

Authors (Year)	Study Population	Mean Age (SD)	N (%) Female	N (%) Race/Ethnicity	Other Characteristics
	materials, or any other factor that would preclude full participation in study, unable or unwilling to get hearing aids if needed.				
Nyenhuis et al. (2013)[50]	Adults with idiopathic tinnitus recruited from newspaper and radio advertisements, otolaryngology offices, and outpatient clinics. *Inclusion:* Age 18 to 75 years old with idiopathic tinnitus for 2 to 26 weeks, internet access. *Exclusion:* Receiving other tinnitus-related psychological treatment.	48.5 (12.8)	132*(43*)	NR	*Tinnitus Duration* Mean (SD) duration in months: 3.2 (1.9) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled
Robinson et al. (2008)[53]	Adults with distressing tinnitus referred by medical provider, self-referred, or recruited with flyers. *Inclusion:* Self-reported distress of any severity due to tinnitus. *Exclusion:* Unable to attend or participate in group sessions for physical or psychological reasons such as psychosis or dementia.	55.0 (11.3)	31 (48)*	White: 57* (88)	*Tinnitus Duration* Mean duration: 11.0 years *Hearing Loss* Hearing loss was not required or excluded, and no mention of this characteristic was made in describing the study population
Sadlier et al. (2008)[56]	New patients at a tinnitus clinic with intrusive tinnitus. *Inclusion:* Intrusive tinnitus *Exclusion:* Treatable cause of tinnitus (e.g., otitis media), nonbothersome tinnitus.	Control: 54.3 (15.3) CBT: 60 (14.6)	Control: 6 (55*) CBT: 11 (79*)	NR	*Tinnitus Duration* Mean (SD) in years Control: 8 (6.3) CBT: 8.5 (6.9) *Hearing Loss* Hearing loss was not required or excluded, and no mention of this characteristic was made in describing the study population
Weise et al. (2016)[48]	Adults 18 or older with confirmed subjective tinnitus recruited via health-related websites, public media, and self-help groups. *Inclusion:* Adults 18 or older with confirmed subjective tinnitus (by an ear, nose, throat specialist) that is reportedly present for most of the time per day for at least 6 months. Score of 38 or higher on the THI or 13 or higher on the Mini-TQ. No tinnitus-specific psychological treatment within the previous 2 years. Access to a computer with an Internet	Control: 47.5 (14.1) CBT: 47.81 (12.3)	74* (60*)	NR	*Tinnitus Duration* Mean (SD) duration in years Control: 7.3 (9.3) CBT: 7.3 (6.8) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled

Authors (Year)	Study Population	Mean Age (SD)	N (%) Female	N (%) Race/Ethnicity	Other Characteristics
	connection; sufficient reading and writing skills, availability of 2 or more hours per week for 10 weeks to participate. *Exclusion:* Tinnitus due to a medical condition; severe medical or psychiatric condition and acute suicidality.				
Weise et al. (2008)[54]	Adults with tinnitus for more than 6 months causing severe or serious annoyance recruited by newspaper articles and the German Tinnitus Association website. *Inclusion:* Age 16 to 75 years, tinnitus for more than 6 months, TQ score > 47. *Exclusion:* Only mild tinnitus annoyance, Meniere's disease, psychosis or seriously disabling brain injury, dementia.	Control: 52.9 (11.9) CBT: 49.5 (11.8)	Control: 26 (44.1) CBT: 23 (44.2)	NR	*Tinnitus Duration* Mean (SD) in years Control: 7.1 (8.3) CBT: 5.7 (5.2) *Hearing Loss* Hearing loss was not required or excluded, and no mention of this characteristic was made in describing the study population
Zachriat et al. (2004)[58]	Adults with tinnitus for 3 months or more and a tinnitus disability score > = 25 recruited by newspaper ads. *Inclusion:* Tinnitus duration of at least 3 months, hearing capacity sufficient for group communication, tinnitus questionnaire score > = 25, sufficient hearing capacity for communication within groups. *Exclusion:* Treatable organic causes of tinnitus, Meniere disease, ongoing psychotherapy or masker treatment.	Control: 56.1 (10.6) CBT: 53.8 (11.8) TRT: 51.6 (11.0)	Control: 5 (26)* CBT: 11 (41)* TRT: 10 (33)*	NR	*Tinnitus Duration* Tinnitus duration in months (SD) Control: 90.2 (79.0) CBT: 68.5 (61.9) TRT: 65.4 (64.3) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled
Zenner et al. (2013)[65]	Adults with non-acute, persistent and stable tinnitus for at least 11 weeks recruited from hospital and referral centers. *Inclusion:* Adults with persistent and stable tinnitus for more than 11 weeks, normal findings using an ear microscope, normal tympanic membrane mobility and stapedial reflex, ability to fill out relevant questionnaires, and gap between the sound pressure level in the audiometric tinnitus matching (tinnitus level above threshold) and the tinnitus loudness using the TLS.	Median 49 (Range 14 to 78)	98 (34)	NR	*Tinnitus Duration* N (%) with duration of tinnitus in categories 4 to 12 mos. Control: 14 (12) CBT: 83 (50) > 12 mos. Control: 106 (88) CBT: 82 (50) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled

Authors (Year)	Study Population	Mean Age (SD)	N (%) Female	N (%) Race/Ethnicity	Other Characteristics
	Exclusion: Non-persistent tinnitus (pulsatile, intermittent) or tinnitus with a concomitant symptom of a known systemic disease (e.g., Ménière's disease), known retrocochlear hearing defect, conductive hearing loss exceeding 10 dB at 2 or more frequencies, ear canal.				

Abbreviations: BDI = Beck Depression Inventory; CBT = cognitive behavioral therapy; ENT = ear, nose and throat; Mini-TQ = Mini-Tinnitus Questionnaire; NR = not reported; RCT = randomized controlled trial; SD = standard deviation; TFI = Tinnitus Functional Index; THI = Tinnitus Handicap Inventory; TLS = Tinnitus Loudness Score; TQ = Tinnitus Questionnaire; TRQ = Tinnitus Reaction Questionnaire; U.K. = United Kingdom; U.S. = United States.; VA = Veterans Administration; VAS = Visual Analogue Scale.

Table D3c. Intervention Characteristics for Included Cognitive Behavioral Therapy Interventions

Author Year	Duration of Intervention	Eligible Comparators (N randomized)	Eligible Interventions (N randomized)	Fidelity
Abbott et al. (2009)[64]	6 weeks	**Information-Only Control (24)** Basic tinnitus psychoeducational information but without the CBT components. Weekly contact from therapists via email to provide passwords for accessing the content each week.	**Internet-based CBT (32)** Ten components presented in 6 modules, one module each week. Modules included relaxation techniques, imagery training, and attention control. Participants received weekly homework assignments, kept weekly diaries and received weekly emails from study trained psychologists.	Mean (SD) number of weeks completed Control: 4.8 (2.5) CBT: 2.1 (2.7)
Andersson et al. (2005)[57]	6 weeks	**Waitlist Control (11)** Nothing for 5 weeks and then treatment	**Group-based CBT (12)** 6 weekly 2-hour small group sessions with information on tinnitus, applied relaxation, cognitive restructuring, behavioral activation, positive imagery, environmental sound enrichment, hearing tactics, and relapse prevention.	NR
Andersson et al. (2002)[60]	6 weeks	**Waitlist Control (64)** No treatment for at least 6 weeks, then offered treatment	**Internet-based CBT (53)** Internet-based CBT self-help manual with 6 weekly modules on topics including tinnitus treatment, applied relaxation, hearing tactics, sound enrichment, controlled breathing, cognitive therapy, negative thoughts and beliefs related to tinnitus, differential relaxation, behavioral sleep management, rapid relaxation, and relapse prevention. All modules included homework and weekly reports to be submitted online.	NR
Beukes et al. (2018)[46] Beukes et al. (2018)[192]	8 w	**Attention-only Control (73)** Weekly monitoring	**Internet-based CBT (73)** CBT delivered via internet in 2 to 3 modules per week over 8 weeks. Overall there were 16 "recommended" and 5 "optional" modules. The modules encompassed CBT principles including goal setting and time setting, and content included topics including cognitive restructuring and and imagery techniques.	NR
Henry et al. (2018)[45]	5 weeks for active intervention, booster at 3 and 6 months	**Waitlist control (104)** Delayed intervention; participants did not receive an intervention workbook until after 6-month outcomes were collected.	**Individual, telephone-based CBT (101)** Participants received a workbook and 5 telephone appointments with audiologist and psychologist beginning 13 days after study initiation that include skills education for self-management including use of therapeutic sound, and coping skills from cognitive behavioral therapy. Participants can also receive more in-depth evaluation and more individualized support if needed.	Mean (SD) telephone appointments per participant: 6.2 (2.0) Mean (SD) contact time in minutes: 293.7 (88.5) N(%) participants with 0 to 3 appointments: 12 (11.9)

Author Year	Duration of Intervention	Eligible Comparators (N randomized)	Eligible Interventions (N randomized)	Fidelity
Henry et al. (2017)[47]	5 weeks	**Waitlist control (150)** Waitlist before receiving PTM after the intervention period	**Group-based CBT (150)** Skills education comprised of 5 weekly group workshops: 2 with an audiologist and 3 with a psychologist. Based on CBT principles. Participants could receive advanced evaluation and treatment depending on their needs, Level 4 included an in-depth evaluation and Level 5 included individualized support.	NR
Henry et al. (1998)[63]	8 weeks	**Waitlist control (12)** Delayed treatment	**Group-based CBT (12)** Termed by study authors as 'cognitive restructuring', consisted of techniques to distinguish positive, negative, and neutral thoughts and employ coping strategies. Consisted of 8 weekly sessions of 90 minutes, with structured home assignments for practice of techniques.	NR
Henry et al. (1996)[62]	6 weeks	**Waitlist control (20)** Delayed treatment	**Group-based CBT (20)** Participants received one 90-minute session weekly for 6 weeks in small groups of 5 to 7 participants; training in attention diversion, mental imagery, cognitive restructuring, and tinnitus education delivered through audiocasettes and written materials.	NR
Hesser et al. (2012)[51]	8 weeks	**Online discussion forum control (32)** Moderated online discussion forum targeting tinnitus-related problems.	**Internet-based CBT (32)** Guided internet delivered materials and a therapist who provided support and directed therapeutic activities. Eight modules were presented, one per week, for 8 weeks. Tinnitus-specific techniques included applied relaxation, positive imagery, attention training, cognitive restructuring, exposure, and use of background sounds. Interventions targeting specific problem areas (sleep, problem solving, hearing tactics) were optional.	5 (16%) in CBT group did not complete a single module.
Jasper et al. (2014)[49] Conrad et al. (2015)[193]	10 weeks	**Online discussion forum control (44)** Active control group; a 10-week internet discussion forum monitored by a therapist in which participants could reply to weekly discussion topics but did not receive any intervention.	**Group-based CBT (43)** Ten 90-minute weekly in-group group sessions during which participants received education and training on topics that included relaxation techniques, cognitive restructuring, and attentional processes in tinnitus perception. Participants received written materials, exercises, and homework assignments meant to enhance understanding and to transfer the new information into their daily routine. Participants interacted with a therapist at every session.	Mean (SD) number of sessions attended in Group CBT group: 7.33 (2.95); 61% completed at least 80% of treatment Mean (SD) number of completed modules in the internet CBT group: 9.05 (3.27); 86% completed at least 80% of treatment

Author Year	Duration of Intervention	Eligible Comparators (N randomized)	Eligible Interventions (N randomized)	Fidelity
			Internet-based CBT (41) Ten-week program of internet-delivered materials broken out into 12 core modules with 6 optional modules. The core modules covered topics including cognitive restructuring, attention shift, and avoidance behavior, and the optional modules covered topics such as sleep management and concentration management. Participants e-mailed a therapist each week about progress and could receive feedback, support, and recommendations on proceeding.	
Kaldo et al. (2007)[55]	6 weeks	**Waitlist control (38)** Nothing for 6 weeks, then sent self-help book and call from study therapist	**Book-guided CBT (34)** Participants mailed 230 page CBT-based self-help book including tinnitus-specific information (e.g., impact of tinnitus distress, advice on noise sensitivity and hearing impairments), included mandatory tools with detailed instructions on how to tailor the tools and tracking sheets to record effort and results, 7 weekly phone calls over a period of 6 weeks with the same therapist focused on evaluating treatment progress and providing advice regrading how to move forward.	NR
Kroner-Herwig et al. (2003)[59]	NR	**Waitlist control (20)** No treatment	**Group-based CBT (43)** Referred to as tinnitus coping training, consisted of 11 small group sessions from 90 to 120 minutes based on a training manual with topics including education on tinnitus, relaxation, tinnitus reactions, dysfunctional and functional thoughts, changing emotional context of tinnitus, habituation exercises, coping, and problem solving.	NR
Malouff et al. (2010)[52]	8 weeks	**Waitlist control (78)** Waitlist control group	**Book-guided CBT CBT (84)** Participants were mailed a self-help book based on CBT principles; book included specific exercises and was derived from an effective standard clinical psychological intervention project. Participants advised to read the book over the subsequent 6 weeks.	Participants were surveyed at month 2 how much they had read the self-management guide; participants on average read 82% of the book.
Martz et al. (2018)[61]	5 weeks	**Waitlist Control (10)** No intervention during study then offered intervention after final assessments completed	**Group-based CBT (10)** 5 weekly sessions including 3 CBT sessions and 2 tinnitus-related audiological education sessions lasting up to 2 hours each. CBT sessions included education on the CBT cycle, relaxation, discussion about thought errors,	Only 4 of the 10 allocated participants actually attended the sessions.

Author Year	Duration of Intervention	Eligible Comparators (N randomized)	Eligible Interventions (N randomized)	Fidelity
			and steps to correct thought errors. Audiological sessions included education on why and how to use sound enrichment techniques, how to create a plan for using sound in specific situations, and how to protect hearing form further damage. Participants given an intervention-specific self-help workbook.	
Nyenhuis et al. (2013)[50]	Information-only control, Internet CBT, Bibliotherapy CBT: 12 weeks Group CBT: 4 weeks	**Information-only control (77)** Sent an 11-page booklet with information about the auditory system, triggers for tinnitus, and medical treatment options.	**Book-guided CBT (77)** Sent a 67-page tinnitus coping training manual and compact disc recording regarding progressive muscle relaxation training. Manual contains multiple choice self-tests to check comprehension at regular intervals. Exercises offered at the end of each lesson. No contact with a therapist; this was a self-management intervention. **Internet-based CBT (79)** Same 67-page tinnitus coping training manual as used in bibliotherapy arm, but accessed via website, and access to the progressive muscle relaxation training was via a downloadable MP-3 sound recording. No contact with a therapist; this was a self-management intervention. **Group-based CBT (71)** Four 2-hour weekly meetings moderated by 3 psychologists based on the same tinnitus coping strategies manual.	NR
Robinson et al. (2008)[53]	8 weeks	**Waitlist control (27)** Nothing for 8 weeks and then began treatment	**Group-based CBT (38)** 8 weekly sessions of manualized group CBT that emphasized cognitive restructuring, increasing pleasant activities, relaxation techniques, and goal setting	26 (68*) participants in the CBT group completed at least 6 of 8 sessions.
Sadlier et al. (2008)[56]	NR	**Waitlist control (11)** Nothing for 3 months; then received treatment	**Individual-based CBT (14)** Individually tailored CBT and mindfulness meditation delivered over 4 one hour sessions that focused on exploring patient's model of tinnitus, cognitive reconstruction, behavioral adaptation, mindfulness meditation, sleep facilitation, and applying techniques to cue control situations	NR
Weise et al. (2016)[48]	10 weeks	**Online discussion forum control (62)** A confidential, therapist moderated online discussion forum for 10 weeks to control for nonspecific effects of intervention	**Internet-based CBT (62)** An online self-guided program of 12 mandatory and 6 optional text modules. Participants were to complete the mandatory modules and could choose the optional	N (%) completed intervention Control 61 (98) CBT: 59 (95)

Author Year	Duration of Intervention	Eligible Comparators (N randomized)	Eligible Interventions (N randomized)	Fidelity
		(e.g., increased attention). Tinnitus topics were posted for discussion but no strategies to improve tinnitus-related distress were	modules to complete. Therapists were available online to address direct questions (up to 10 minutes/week). Based on an existing well-established CBT self-help manual. Each module was structured in same way: theory and general information, exercises, worksheets, and solutions for common problems.	
Weise et al. (2008)[54]	3 months	**Waitlist control (67)** Nothing for 3 months and then received treatment	**Individual-based CBT (63)** Twelve 1-hour individual therapy sessions including CBT and biofeedback behavioral intervention components. Biofeedback components included muscle relaxation training and threshold training. CBT components included information on tinnitus and hearing, the influence of stress, and the importance of cognitions.	NR
Zachriat et al. (2004)[58]	CBT: 12 weeks TRT: 24 weeks	**Education only control (23)** One education session on the physiology and psychology of tinnitus, comparable to first education session in CBT and TRT	**Group-based CBT (29)** Termed tinnitus coping training by study authors; participants educated and counseled on physiology and psychology of tinnitus, relaxation exercises, attention distraction strategies, CBT-based approaches to identify and modify cognitive and emotional responses to tinnitus, avoidance behavior, and relapse coping. Consisted of 11 weekly group sessions (6-8 participants) each 90-120 minutes in length **Tinnitus Retraining Therapy (31)** Termed habituation training by study authors; participants received group-based counseling modeled on tinnitus retraining therapy; focused on physiological and psychological distress of tinnitus as well as peripheral and central neuronal mechanisms involved in tinnitus perception, also received wide-band sound generators adapted individually by audiologist. Participants instructed to use the generators at least 6 hours per day. Five sessions total, each session held every 4 to 6 weeks over a total span of 6 months.	NR
Zenner et al. (2013)[65]	NR	**Waitlist control (120)** Participants at one of 5 participating centers received delayed treatment.	**Individual-based CBT (166)** Provided at 4 of the 5 participating centers, a clinician-delivered individual CBT disease management plan made electronically available to clinicians who individualized according to patient characteristics.	NR

Abbreviations: CBT = cognitive behavioral therapy; NR = not reported; PTM = Progressive Tinnitus Management; TRT = tinnitus retraining therapy; SD = standard deviation.

Table D3d. Efficacy Outcomes for Included Cognitive Behavioral Therapy Interventions

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
Abbott et al. (2009)[64] Information-only control (24) Internet-based CBT (32)	Tinnitus Reaction Questionnaire No	Between-group difference in change in score immediately post-treatment: NR; *P* = 0.22
	VAS for tinnitus loudness No	Between-group difference in change in score immediately post-treatment: NR; *P* = 0.16
	VAS for tinnitus annoyance No	Between-group difference in change in score immediately post-treatment: NR; *P* = 0.86
	VAS for tinnitus control No	Between-group difference in change in score immediately post-treatment: NR; *P* = .39
	VAS for sleep quality No	Between-group difference in change in score immediately post-treatment: NR; *P* = 0.43
	Depression, Anxiety, and Stress Scale No	Between-group difference in change in score immediately post-treatment: NR; *P* = 0.80
	World Health Organization Quality of Life No	Between-group difference in change in score immediately post-treatment: NR; *P* = 0.68
Andersson et al. (2005)[57] Waitlist control (11) Group-based CBT (12)	Tinnitus Reaction Questionnaire No	Mean between-group difference in change in score at 5w: -10.3* (95% CI, NR); *P* = 0.014 Clinically significant improvement (50% decrease in mean TRQ score) Control: 0 (0) Group-based CBT: 5* (42) *P* = 0.049 RD*: 37.3% (95% CI, 7.0% to 67.6%) RR*: 96 (95% CI, 0.59 to 156.4)
	VAS for tinnitus loudness No	Data presented in figures only, actual values NR Mean between-group difference in change in score at 5w: NR (95% CI, NR); *P* NS
	VAS for tinnitus annoyance No	Data presented in figures only, actual values NR Mean between-group difference in change in score at 5w: NR (95% CI, NR); *P* = 0.0004
	Hospital Anxiety and Depression Scale-Depression No	Mean between-group difference in change in score at 5w: -1.1 (95% CI, NR); *P* NS
	Hospital Anxiety and Depression Scale-Anxiety No	Mean between-group difference in change in score at 5w: -0.9 (95% CI, NR); *P* NS

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
	Anxiety Sensitivity Index No	Mean between-group difference in change in score at 5w: -8.5 (95% CI, NR); *P* = 0.003
	Sleep Quality No	Data presented in figures only, actual values NR Mean between-group difference in change in score at 5w: NR (95% CI, NR); *P* NS
Andersson et al. (2002)[60] Waitlist control (64) Internet-based CBT (53)	Tinnitus Reaction Questionnaire Yes	Mean between-group difference in change in score at 6 w: -12.5* (95% CI, NR), *P* = 0.002 favoring CBT N (%) with clinically significant reduction (50% or more score decrease)-intent to treat analysis Control: 2 (3*) Internet-based CBT: 7 (13) *P* = 0.29
	VAS for tinnitus loudness No	Mean between-group difference in change in score at 6 w: -0.6* (95% CI, NR), *P* = 0.04 favoring CBT
	VAS for tinnitus annoyance No	Mean between-group difference in change in score at 6 w: -1.4* (95% CI, NR), *P* = 0.001 favoring CBT
	VAS for tinnitus control No	Mean between-group difference in change in score at 6 w: 0.9* (95% CI, NR), *P* = 0.05
	VAS for sleep quality No	Mean between-group difference in change in score at 6 w: 0.6* (95% CI, NR), *P* = 0.10
	Hospital Anxiety and Depression Scale-Depression No	Mean between-group difference in change in score at 6 w: -3.2* (95% CI, NR), *P* = 0.002
	Hospital Anxiety and Depression Scale-Anxiety No	Mean between-group difference in change in score at 6 w: -2.2* (95% CI, NR), *P* = 0.004
	Anxiety Sensitivity Index No	Mean between-group difference in change in score at 6 w: -4.5* (95% CI, NR), *P* = 0.015
Beukes et al. (2018)[46] Beukes et al. (2018)[192] Control (73) Internet-based CBT (73)	Tinnitus Functional Index Yes	Reduction in mean (SD) TFI score from baseline to post-intervention (T0 vs. T1) Control: 5 (3.9) Internet-based CBT: 21 (14.9) Average reduction in points (maximum reduction), baseline to post-intervention: Control: 10-40 (81) Internet-based CBT: higher than baseline to 20 point reduction N (%) of participants achieving clinical significance: Post-intervention: Control: 3* (5), n = 63 Internet-based CBT: 37* (51), n = 72 Mean (SD) difference between groups: Post-intervention: 15.1 (10.6) Between-group Cohen's d (95% CI): 0.7 (95% CI: 0.4 to 1.0)

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
		Between-group effect: 3.9, *P* = 0.05 2 month FU: 3.5 (2.5)
	Insomnia Severity Index No	N (%) reaching clinical significance (ISI score change >9.8) at post-intervention: Control: 3* (4), n = 63 Internet-based CBT: 16* (22), n = 72 Mean (SD) difference between groups: Post-intervention: 3.8 (2.7) Between-group Cohen's d (95% CI): 0.6 (95% CI, 0.2 to 0.9) Between-group effect: 5.4, *P* = 0.02 2 month FU: 2.5 (1.7)
	Generalized Anxiety Disorder-7 No	Mean (SD) difference between groups: Post-intervention: 1.9 (1.3) Between-group Cohen's d (95% CI): 0.3 (95% CI, 0.1 to 0.6) Between-group effect: 0.5, *P* = 0.55 2-month followup: 0.4 (0.3)
	Patient Health Questionnaire-9 No	N (%) reaching clinical significance (score change of 6.4) at post-intervention: Control: 3* (4), n = 63 Internet-based CBT: *12 (16), n = 72 Mean (SD) difference between groups: Post-intervention: 1.9 (1.3) Between-group Cohen's d (95% CI): 0.3 (95% CI, 0.0 to 0.7) Between-group effect: 1.1, *P* = 0.31 2 month FU: 0.4 (0.3)
Henry et al. (2018)[45] Waitlist control (104) Telephone-based Progressive tinnitus management (101)	Tinnitus Handicap Inventory No	Mean (SD) change at 3 mo,; N Control: -0.1 (11.9); 99 Tele-PTM: -13.5 (17.5); 84 Effect size: 0.91 (0.60 to 1.21) Between-group difference*: -13.4 (95% CI, -17.7 to -9.1) Mean (SD) change at 6 mo; N Control: -0.5 (12.8); 94 Tele-PTM: -16.0 (18.8); 81 Effect size: 0.98 (0.66 to 1.29) Between-group difference*: -15.5 (-20.2 to -10.8); *P*<0.001 N (%) with 20 point or more reduction at 6 mo Control: 8 (8) Tele-PTM: 36 (44) RD* 36.0 (95% CI, 23.9 to 48.1); *P*<0.001

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
		RR* 5.5 (95% CI, 2.7 to 11.4)
	Tinnitus Functional Index Yes	Mean (SD) change at 3 mo; N Control: -0.6 (11.9); 99 Tele-PTM: -17.0 (18.7); 86 Effect size: 1.06 (0.75 to 1.37) Between-group difference*: -16.4 (95% CI, -20.9 to -11.9); *P*<0.001 Mean (SD) change at 6 mo; N Control: -1.3 (14.1); 94 Tele-PTM: -20.9 (18.4); 82 Effect size: 1.20 (95% CI, 0.87 to 1.51) Between-group difference*: -19.6 (95% CI, -24.5 to -14.8), *P*<0.0001 N (%) achieving a 13-point or more reduction at 6 mo Control: 22* (23) Tele-PTM: 52* (64) RD* 40.0% (95% CI, 26.5% to 53.5%); *P*<0.001 RR* 2.7 (95% CI, 1.8 to 4.0)
	Hospital Anxiety and Depression Scale-Depression No	Mean (SD) change at 6 mo, N Control: 0.16 (3.5); 93 Tele-PTM: -1.52 (3.3); 81 Effect size 0.50 (95% CI, 0.19 to 0.80) Between-group difference*: -1.7 (95% CI, -2.7 to -0.66); *P* = 0.001
	Hospital Anxiety and Depression Scale-Anxiety No	Mean (SD) change at 6 mo, N Control: -0.27 (2.8); 93 Tele-PTM: -1.92 (3.4); 81 Effect size: 0.53 (95% CI, 0.22 to 0.83) Between-group difference*: -1.7 (95% CI, -2.6 to -0.72); *P*<0.001
	Epworth Sleepniess Scale No	Mean (SD) change at 6 mo, N Control: -0.14 (4.4); 93 Tele-PTM: -0.85 (4.0); 81 Effect size: 0.17 (95% CI, -0.13 to 0.47) Between-group difference:*: -0.7 (95 %CI, -2.0 to 0.56); *P* = 0.27
Henry et al. (2017)[47] Waitlist control (150) Group-based progressive tinnitus management (150)	Tinnitus Handicap Inventory No	Mean (SD) change at 6 mo; N Control: 2.3 (17.2); 121 Group-based PTM: -4.3 (17.8); 111 Effect size: 0.38 (95% CI, 0.12 to 0.64) Between-group difference*: -6.6 (-11.1 to -2.1); *P* = 0.004 N (%) with 20-point or more reduction at 6 mo

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
		Control: 11 (9.1) Group-based PTM: 19 (17.1) *P*>0.05 RD* 8.0% (95% CI, -0.65% to 16.7%) RR* 1.9 (95% CI, 0.94 to 3.8)
	Tinnitus Functional Index Yes	Mean (SD) change at 6 mo; 231 Control: 0.8 (17.5); 119 Group-based PTM: -5.7 (18.8); 112 Effect size: 0.36 (95% CI, 0.10 to 0.62) Between-group difference*: -6.5 (95% CI, -11.2 to-1.8); *P* = 0.007 N (%) with 13 point or more reduction at 6 mo Control: 21 (17.6) Group-based PTM: 38 (33.9) *P* = 0.005 RD* 16.3% (95% CI, 5.2% to 27.4%) RR* 1.9 (95% CI, 1.2 to 3.1)
Henry et al. (1998)[63] Waitlist control (12) Group-based CBT (12)	Tinnitus Handicap Questionnaire No	Mean (SD) score at baseline Control: 42.1 (21) Group-based CBT: 42.4 (12.9) Mean (SD) score at post-intervention Control: 35.9 (14.7) CBT: 36.5 (10.9) Between-group difference in change in score post-intervention: 0.3*, *P* NR
	Tinnitus Reaction Questionnaire No	Mean (SD) score at baseline Control: 31.9 (17) Group-based CBT: 31.4 (11.3) Mean (SD) score at post-intervention Control: 27.6 (14.9) CBT: 19.3 (9.5) Between-group difference in change in score post-intervention: -7.8*, *P* NR
	Tinnitus Effects Questionnaire No	Emotional Distress Subscale Mean (SD) score at baseline Control: 11.5 (2.4) Group-based CBT: 10.8 (1.8) Mean (SD) score at post-intervention Control: 11.8 (2.2) Group-based CBT: 8.9 (0.9)

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
		Between-group difference in change in score post-intervention: -2.2*, *P* NR Irrational Beliefs Subscale Mean (SD) score at baseline Control: 7.7 (1.8) Group-based CBT: 6.9 (1.4) Mean (SD) score at post-intervention Control: 8.7 (2.0) Group-based CBT: 7 (1.6) Between-group difference in change in score post-intervention: -0.9*, *P* NR
	Tinnitus Cognitions Questionnaire No	Mean (SD) score at baseline Control: 47.4 (18.0) Group-based CBT: 45.9 (11.0) Mean (SD) score at post-intervention Control: 38.7 (17.1) Group-based CBT: 27.0 (12.7) Between-group difference in change in score post-intervention: -10.2*, *P* NR
	Tinnitus Coping Strategies Questionnaire No	Frequency Subscale Mean (SD) score at baseline Control: 37.3 (11.5) Group-based CBT: 34.1 (13.9) Mean (SD) score at post-intervention Control: 34.9 (15) Group-based CBT: 39.3 (10.8) Between-group difference in change in score post-intervention: 7.6*, *P* NR Benefits Subscale Mean (SD) score at baseline Control: 33.5 (12.8) Group-based CBT: 27.7 (17.4) Mean (SD) score at post-intervention Control: 33.8 (18.4) Group-based CBT: 34.4 (11.8) Between-group difference in change in score post-intervention: 6.4*, *P* NR
	Beck Depression Inventory No	Mean (SD) score at baseline Control: 8.4 (3.9) Group-based CBT: 10.5 (4.3) Mean (SD) score at post-intervention Control: 10.4 (4.6)

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
		Group-based CBT: 8.8 (4.3) Between-group difference in change in score post-intervention: -3.7*, *P* NR
Henry (1996)[62] Waitlist control (20) Group-based CBT (20)	Tinnitus Handicap Questionnaire No	Mean between-group difference in change in score immediately post-treatment: -11.3* (95% CI, NR) ; *P* NR
	Tinnitus Reaction Questionnaire No	Mean between-group difference in change in score immediately post-treatment: -8.0 * (95% CI, NR); *P* NR
	Tinnitus Effects Questionnaire No	Emotional Distress Subscale Mean between-group difference in change in score immediately post-treatment: -1.8 * (95 %CI, NR); *P* NR Irrational Beliefs Subscale Mean between-group difference in change in score immediately post-treatment: -1.8 * (95 %CI, NR); *P* NR
	Tinnitus Cognitions Questionnaire No	Mean between-group difference in change in score immediately post-treatment: -11.7* (95 %CI, NR); *P* NR
	Tinnitus Coping Strategies Questionnaire No	Frequency Subscale Mean between-group difference in change in score immediately post-treatment: 10.7* (95% CI, NR); *P* NR Benefits Subscale Mean between-group difference in change in score immediately post-treatment: 10.2* (95% CI, NR); *P* NR
	Beck Depression Inventory No	Mean between-group difference in change in score immediately post-treatment: -2.0* (95% CI, NR); *P* NS
Hesser et al. (2012)[51] Control (online discussion forum) (32) Internet-based CBT (32)	Tinnitus Handicap Inventory Unsure	Baseline Control: 60.9 (14.8); N = 32 Internet-based CBT: 60.2 (14.6); N = 32 8-week followup Control 49.9 (16.1); N = 32 Internet-based CBT: 38.9 (19.7); N = 30 Cohen's d = 0.70; *P* = 0.006 favoring CBT N (%) participants meeting criteria for reliable change and high end-state functioning Control: 5 (16) Internet-based CBT: 14 (44) P = 0.014, favoring CBT
	Tinnitus Acceptance Questionnaire Unsure	Baseline Control: 32.5 (9.9); N = 32 Internet-based CBT: 31.9 (9.4); N = 32 8-week followup Control: 36.8 (11.0); N = 32

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
		Internet-based CBT: 40.5 (8.9); N = 30 Cohen's d = 0.45; *P* = 0.075
	Hospital Anxiety and Depression Scale-Depression Unsure	Baseline Control: 6.0 (3.4); N = 32 Internet-based CBT: 6.0 (3.2); N = 32 8-week followup Control: 4.6 (3.3); N = 32 Internet-based CBT: 3.4 (3.3); N = 30 Cohen's d 0.39 to 0.40, *P*>..10
	Hospital Anxiety and Depression Scale-Anxiety Unsure	Baseline Control: 8.2 (3.9); N = 32 Internet-based CBT: 8.4 (3.7); N = 32 8-week followup Control: 6.8 (4.0); N = 32 Internet-based CBT: 4.7(3.4); N = 30 Cohen's d = 0.68; *P* = 0.008, favoring CBT
	Perceived Stress Scale Unsure	Baseline Control: 27.9 (7.9); N = 32 Internet-based CBT: 27.4 (7.3); N = 32 8-week followup Control: 25.8 (7.9); N = 32 Internet-based CBT: 22.4 (7.1); N = 30 Cohen's d 0.39 to 0.40, *P*>..10
	Insomnia Severity Index Unsure	Baseline Control: 13.8 (6.5); N = 32 Internet-based CBT: 14.7 (6.3); N = 32 8-week followup Control: 11.2 (7.0); N = 32 Internet-based CBT: 9.9 (6.9); N = 30 Cohen's d 0.39 to 0.40, *P*>..10
	Quality of Life Inventory Unsure	Baseline Control: 2.0 (1.6); N = 32 Internet-based CBT: 1.9 (1.8); N = 32 8-week followup Control:2.3 (1.5); N = 32 Internet-based CBT: 2.5 (1.6); N = 30 Cohen's d 0.45, *P* = 0.08

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
Jasper et al.(2014)[49] Conrad et al. (2015)[193] Discussion forum control (44) Group-based CBT(43) Internet-based CBT (41)	Tinnitus Handicap Inventory Yes	Internet-based CBT vs. Control Between-group difference in change in score immediately post-treatment NR; *P* = 0.001; Effect size (Hedge's g) = 0.56 (95% CI, 0.12 to 0.99) Group-based CBT vs. control Between-group difference in change in score immediately post-treatment NR; *P*<0.001; Effect size (Hedge's g) = 0.69 (95% CI, 0.25 to 1.12)
	Tinnitus Acceptance Questionnaire No	Internet-based CBT vs. Control Between-group difference in change in score immediately post-treatment NR; *P* = 0.042; Effect size (Hedge's g) = 0.38 (95% CI, -0.05 to 0.80) Group-based CBT vs. control Between-group difference in change in score immediately post-treatment NR; *P*<0.011; Effect size (Hedge's g) = 0.39 (95% CI, -0.04 to 0.81)
	Mini-Tinnitus Questionnaire Yes	Internet-based CBT vs. Control Between-group difference in change in score immediately post-treatment NR; *P*<0.001; Effect size (Hedge's g) = 0.65 (95% CI, 0.21 to 1.09) Group-based CBT vs. control Between-group difference in change in score immediately post-treatment NR; *P*<0.001; Effect size (Hedge's g) = 0.93 (95% CI, 0.49 to 1.37)
	Hospital Anxiety and Depression Scale-Depression No	Internet-based CBT vs. Control Between-group difference in change in score immediately post-treatment NR; *P* = 0.105; Effect size (Hedge's g) = 0.24 (95% CI, -0.19 to 0.66) Group-based CBT vs. control Between-group difference in change in score immediately post-treatment NR; *P* = 0.078; Effect size (Hedge's g) = 0.26 (95% CI, -0.16 to 0.68)
	Hospital Anxiety and Depression Scale-Anxiety No	Internet-based CBT vs. Control Between-group difference in change in score immediately post-treatment NR; *P* = 0.105; Effect size (Hedge's g) = 0.24 (95% CI, -0.02 to 0.84) Group-based CBT vs. control Between-group difference in change in score immediately post-treatment NR; *P*<0.011; Effect size (Hedge's g) = 0.39 (95% CI, -0.03 to 0.82)
	Insomnia Severity Index No	Internet-based CBT vs. Control Between-group difference in change in score immediately post-treatment NR; *P*<0.001; Effect size (Hedge's g) = 0.64 (95% CI, 0.20 to 1.07) Group-based CBT vs. control Between-group difference in change in score immediately post-treatment NR; *P* = 0.001; Effect size (Hedge's g) = 0.69 (95% CI, 0.10 to 0.95)
Kaldo et al. (2007)[55]	Tinnitus Handicap Inventory	Mean between-group difference in change in score at 6 w: -8.8; *P* <0.001 favoring CBT

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
Waitlist control (38) Book-guided CBT (34)	No	
	Tinnitus Reaction Questionnaire Yes	Mean between-group difference in change in score at 6 w: -11.6 *, *P* <0.001 favoring CBT Between-group effect size d = 0.42 N (%) with clinically significant reduction Control: 2 (5) Book-guided CBT: 11 (32) *P* = 0.003
	VAS for tinnitus loudness No	Mean between-group difference in change in score at 6 w: -0.8* ;*P* = 0.012 favoring book-guided CBT
	VAS for distress No	Mean between-group difference in change in score at 6 w: -1.2*, *P* <0.001 favoring book-guided CBT
	VAS for stress No	Mean between-group difference in change in score at 6 w: -0.3*; *P* = .36
	Hospital Anxiety and Depression Scale-Depression No	Mean between-group difference in change in score at 6 w: -1.8*, *P* = 0.024 favoring book-guided CBT
	VAS for tinnitus control No	Mean between-group difference in change in score at 6 w: -2.1*, *P* = 0.002 favoring book-guided CBT
	Insomnia Severity Index No	Mean between-group difference in change in score at 6 w: -3.0* (95% CI, NR), *P* < .001
Kroner-Herwig et al. (2003)[59] Waitlist control (20) Group-based and Individual-based CBT (43)	Tinnitus Questionnaire No	Immediately post-treatment Mean between-group difference in change in score: -9.2* (95% CI, NR); *P* <0.01
	Tinnitus Disability Questionnaire No	Immediately post-treatment Mean between-group difference in change in score: -0.5* (95% CI, NR); *P* NS
	VAS for tinnitus loudness No	Immediately post-treatment Mean between-group difference in change in score: -0.2* (95% CI, NR); *P* NS
	VAS for tinnitus control No	Immediately post-treatment Mean between-group difference in change in score: 2.0* (95% CI, NR); *P*<0.01
	VAS for awareness No	Immediately post-treatment Mean between-group difference in change in score: -0.3* (95% CI, NR); *P* NS
	SCL-90 R (General psychological status) No	Immediately post-treatment Mean between-group difference in change in score: 0.0* (95% CI, NR); *P* NS
	COPE (Coping Inventory) No	Immediately post-treatment Mean between-group difference in change in score: NR (95% CI, NR); *P* < = 0.01, ES 1.04

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
	Allegmeine Depression Scale No	Immediately post-treatment Mean between-group difference in change in score: -0.3* (95% CI, NR); *P* NS
Malouff et al. (2010)[52] Waitlist control (78) Book-guided CBT (84)	Tinnitus Reaction Questionnaire Yes	Mean (SD) between-group change among participants completing post-test measures:-45; *P* = 0.01, d = .28 However, ITT analysis (actual values not provided) reported a *P* = 0.07 for this between-group difference
	General Health Questionnaire12 No	Mean (SD) between-group change among participants completing post-test measures:-1.8; *P* = 0.02, d = .26 No ITT analysis reported.
Martz et al. (2018)[61] Waitlist control group (10) Group-based CBT (10)	COPE: Engagement Coping No	Mean between-group difference in change in score at end of treatment: -4.2* (95% CI, NR), *P* NS Mean between-group difference in change in score at 4w post-treatment: -5.9* (95% CI, NR), *P* NS
	COPE: Disengagement Coping No	Mean between-group difference in change in score at end of treatment: -0.9* (95% CI, NR), *P* NS Mean between-group difference in change in score at 4w post-treatment: 0.6* (95% CI, NR), *P* NS
	COPE: Social Support Coping No	Mean between-group difference in change in score at end of treatment: -2.4* (95% CI, NR), *P* NS Mean between-group difference in change in score at 4w post-treatment: -3.2* (95% CI, NR), *P* NS
Nyenhuis et al. (2013)[50] Information-only control (77) Book-guided CBT (77) Internet-based CBT (79) Group-based CBT (71	Tinnitus Questionnaire Yes	Mean (SD) score at baseline Control: 34.5 (13.0) Book-guided CBT: 39.2 (16.8) Internet-based CBT: 35.8 (13.4) Group-based CBT: 36.9 (14.9) Mean (SD) score at 3-mos. followup Control: 27.4 (18.0) Bibliotherapy: 26.3 (20.4) Internet: 17.6 (12.7) Group: 20.8 (14.7) Between-group difference in change in score from baseline, *P* value, Effect Size (Cohen's d) Book-guided CBT vs. control: -5.8*; *P* NS; 0.24 (-0.7 to 0.56) Internet-based CBT vs. control: -11.1*; *P*<0.001; 1.04 (0.71 to 1.38) favoring intervention Group-based CBT vs. control: -9.0*; *P* <0.001, 0.89 (0.57 to 1.21) favoring intervention Mean (SD) score at 9-mos. followup Control: 25.2 (19.1) Book-guided CBT: 20.8 (16.7) Internet-based: 19.4 (14.8) Group-based: 18.4 (11.6) Between-group difference in change in score from baseline, *P* value, Effect Size (Cohen's d)

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
		Book-guided CBT vs. control: -9.1*; *P*<0.05, 0.39 (0.07 to 0.71) Internet-based CBT vs. control: --7.1*; *P*<0.05, 0.66 (0.34 to 0.99) Group-based CBT vs. control : --9.2*; *P*<0.01, 0.74 (0.41 to 1.08) N (%) with a clinically significant improvement (TQ change of > = 14 points) at 3-mos. followup Control: 12 (15.6*) Book-guided CBT: 31 (40.2*); *P*<0.01 vs. control Internet-based CBT: 46 (58.2*); *P*<0.001 vs. control Group-based CBT: 45 (63.4*); *P*<0.001 vs. control N (%) with a clinically significant improvement (TQ change of > = 15 points) at 9-mos. followup Control: 22 (28.6*) Book-guided CBT: 41(53.2*); *P*<0.05 vs. control Internet-based CBT: 42 (53.2*); *P*<0.05 vs. control Group-based CBT: NR
	Patient Health Questionnaire-Depression (German) No	Mean (SD) score at baseline Control: 5.9 (4.6) Book-guided CBT: 8.2 (5.3) Internet-based CBT: 6.7 (4.2) Group-based CBT: 6.9 (5.6) Mean (SD) score at 3 mos. Control : 5.7 (4.8) Book-guided CBT: 6.4 (5.9) Internet-based CBT: 5.1 (4.5) Group-based CBT: 4.7 (4.8) Between-group difference in score at 3-mos. followup, *P* value, Effect Size (Cohen's d) Book-guided CBT vs. control: -1.6*; *P* NS, 0.15 (-0.17 to 0.46) Internet-based CBT vs. control: -1.4*; *P* NS, 0.38 (0.07 to 0.70) Group-based CBT vs. control: -2.0*; *P*<0.01, 0.61 (0.29 to 0.94) Mean (SD) score at 9 mos. Control: 5.7 (5.1) Book-guided CBT: 6.5 (5.2) Internet-based CBT: 5.9 (5.3) Group-based CBT: 4.8 (3.8) Between-group difference in score at 9-mos. followup, *P* value, Effect Size (Cohen's d) Book-guided CBT: -1.5*; *P* NS, -0.15 (-0.47 –to 0.16) Internet-based CBT: -0.6*; *P* NS, 0.04 (-0.27 to 0.36) Group-based CBT: -1.9*; *P* NS, 0.26 (-0.07 to 0.58)
Robinson et al. (2008)[53]	Tinnitus Handicap Inventory	Between-group difference: NR, *P* NS

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
Waitlist control (27) Group-based CBT (38)	No	
	Tinnitus Handicap Questionnaire No	Between-group difference: NR, *P* NS
	Tinnitus Reaction Questionnaire No	Between-group difference at 8 w: NR, *P* = 0.03 favoring Group-based CBT
	Tinnitus Questionnaire No	Between-group difference: NR, *P* NS
	VAS for tinnitus annoyance No	Between-group difference: NR, *P* NS
	VAS for severity No	Between-group difference: NR, *P* NS
	Beck Depression Inventory No	Between-group difference at 4 mo and 1 yr: NR, *P* = 0.01 favoring Group-based CBT
	SCL-90 R (General psychological status) No	Between-group difference at 8 w, 4 mo, 1 yr: NR, *P* = 0.01 favoring Group-based CBT
	Hamilton Rating Scale for Depression No	Between-group difference: NR, *P* NS
Sadlier et al. (2008)[56] Waitlist control (11) Individual CBT (14)	Tinnitus Questionnaire No	Data presented on figures only, actual values NR Within-group difference from baseline to 3 months Control: *P* NR Individual CBT: *P* <0.003 Between-group differences NR
	Hospital Anxiety and Depression Scale-Depression No	Data presented on figures only, actual values NR No significant difference in either group from baseline to 3 months
	Hospital Anxiety and Depression Scale-Anxiety No	Data presented on figures only, actual values NR No significant difference in either group from baseline to 3 months
	VAS for overall effect No	Data presented on figures only, actual values NR Within-group difference from baseline to 3 months Control: *P* = 0.053 CBT: *P* <0.007

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
		Between-group differences NR
Weise et al. (2016)[48] Discussion forum control (62) Internet-based CBT (62)	Tinnitus Handicap Inventory Yes	Mean (SD) at baseline, N Control: 51.6 (15.2), 62 Internet-based CBT: 53.39 (14.90), 62 Mean (SD) at post-treatment; N Control: 45.8 (15.1), 61 Internet-based CBT: 32.6 (16.5), 58 Between-group difference in mean change*: -15.1 Hedges g effect size: 0.83 (95% CI, 0.47 to 1.20); *P* = 0.002
	Mini-Tinnitus Questionnaire Yes	Mean (SD) at baseline, N Control: 15.7 (3.6), 62 Internet-based CBT: 16.2 (3.5), 62 Mean (SD) at post-treatment; N Control: 13.3 (4.3), 61 Internet-based CBT: 8.5 (4.5), 58 Between-group difference in mean change*: -5.3 Hedges g effect size: 1.08 (95% CI, 0.71 to 1.64); *P*<0.001
	Tinnitus Acceptance Questionnaire No	Mean (SD) at baseline, N Control: 33.9 (10.2), 62 Internet-based CBT: 34.6 (8.9), 62 Mean (SD) at post-treatment; N Control: 36.5 (10.4), 61 Internet-based CBT: 44.0 (9.3), 58 Between-group difference in mean change*: 6.8 Hedges g effect size: 0.76 (95% CI, 0.40 to 1.13); *P* = 0.011
	Hospital Anxiety and Depression Scale-Depression No	Mean (SD) at baseline, N Control: 7.06 (4.13), 62 Internet-based CBT: 7.87 (3.91), 62 Mean (SD) at post-treatment; N Control: 6.66 (3.98), 61 Internet-based CBT: 5.27 (3.72), 58 Between-group difference in mean change*: -2.2 Hedges g effect size: 0.36 (95% CI, 0.01 to 0.72); *P* = 0.66
	Hospital Anxiety and Depression Scale-Anxiety No	Mean (SD) at baseline, N Control: 8.7 (3.2), 62 Internet-based CBT: 9.8 (3.1), 62 Mean (SD) at post-treatment; N

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
		Control: 7.8 (3.3) 61 Internet-based CBT: 6.7 (3.4), 58 Between-group difference in mean change*: -2.3 Hedges g effect size: 0.35 (95% CI, 0.00 to 0.71); *P* NR
	Insomnia Severity Index No	Mean (SD) at baseline, N Control: 12.8 (6.1), 62 Internet-based CBT: 11.6 (5.6), 62 Mean (SD) at post-treatment; N Control: 11.6 (6.4), 61 Internet-based CBT: 7.7 (5.4), 58 Between-group difference*: -2.7 Hedges g effect size: 0.66 (95% CI, 0.30 to 1.02); *P*<0.001
Weise et al. (2008)[54] Waitlist control (67) Individual-based CBT (63)	Tinnitus Questionnaire Yes	Mean between-group difference in change in score: -16.8*; *P*<0.001; Effect size (Hedge's g) = 0.95
	VAS for distress Yes	Mean between-group difference in change in score at 3 mos: -1.1*; *P*<0.01; Effect size (Hedge's g) = 0.45
	Beck Depression Inventory No	Mean between-group difference in change in score at 3 mos: -2.4; *P*<0.01; Effect size (Hedge's g) = 0.12
	SCL-90 R (General psychological status) No	Mean between-group difference in change in score at 3 mos.: -0.2; *P*<0.01; Effect size (Hedge's g) = 0.07
	Tinnitus-Related Control Scale: Helplessness No	Mean between-group difference in change in score at 3 mos.: -5.5; *P*<0.001; Effect size (Hedge's g) = 0.80
	Tinnitus-Related Control Scale: Resourcefullness No	Mean between-group difference in change in score at 3 mos.: 4.8; *P*<0.001; Effect size (Hedge's g) = 0.91
	Tinnitus-Related Control Scale: Resourcefullness No	Mean between-group difference in change in score at 3 mos.: -8.6; *P*<0.001; Effect size (Hedge's g) = 0.81
	Tinnitus-Related Control Scale: Coping No	Mean between-group difference in change in score at 3 mos.: 6.0; *P*<0.001; Effect size (Hedge's g) = 1.12
Zachriat et al. (2004)[58] Education only (active control) (23) Group-based CBT (29) Tinnitus retraining therapy (31)	Tinnitus Questionnaire Yes	Between-group difference in change in score at 15 weeks Group-based CBT: -9.5* (at end of intervention); *P* = 0.018; effect size (d) 0.81 TRT: -8.1* (after 4 of 5 sessions completed); *P* = 0.015; effect size (d) 0.67

Authors (Year) Interventions (N Randomized)	Name of Measure Primary Endpoint (Yes/No/Unsure)	Results
Zenner et al. (2013)[65] Waitlist control (120) Individual-based CBT (166)	Tinnitus Questionnaire No	Median (quartile) change in score (timepoint unspecified) Control: 28 (15 to 46) Individual-based CBT: 13.5 (7 to 23) OR 2.0 (95% CI, 1.6 to 2.5)
	Tinnitus Loudness Score No	Median (quartile) change in score (timepoint unspecified) Control: 3.5 (3 to 4) Individual-based CBT: 2 (1 to 3) OR 2.2 (95% CI, 1.8 to 2.8)
	Tinnitus Annoyance Score No	Median (quartile) change in score (timepoint unspecified) Control: 4 (3 to 5) Individual-based CBT: 1 (1 to 3) OR 2.6 (95% CI, 2.1 to 3.3)
	Tinnitus Change Score Yes	Median (quartile) change in score (timepoint unspecified) Control: 4 (4 to 5) Individual-based CBT: 3 (2 to 3) OR 3.4 (95% CI, 2.6 to 4.5)

Abbreviations: CBT = Cognitive Behavioral Therapy; CI = confidence interval; OR = odds ratio; mos = months; NR = not reported; PTM = Progressive Tinnitus Management; SD = standard deviation; Tele-PTM = Telephone Progressive Tinnitus Management; TRT = Tinnitus Retraining Therapy.

Table D3e. Safety and Cost Outcomes for Included Cognitive Behavioral Therapy Interventions

Authors (Year) Interventions (N Randomized)	Safety Outcomes	Cost Outcomes
Abbott et al. (2009)[64] Information-only control (24) Internet-based CBT (32)	NR	NR
Andersson et al. (2005)[57] Waitlist control (11) Group-based CBT (12)	NR	NR
Andersson et al. (2002)[60] Waitlist control (64) Internet-based CBT (53)	NR	NR
Beukes et al. (2018)[46] Beukes et al. (2018)[192] Control (73) Internet-based CBT (73)	NR	NR
Henry et al. (2018)[45] Waitlist control (104) Telephone-based progressive tinnitus management (101)	NR	NR
Henry et al. (2017)[47] Waitlist control (150) Group-based progressive tinnitus management (150)	NR	NR
Henry et al. (1998)[63] Waitlist control (12) Group-based CBT (12)	NR	NR
Henry et al. (1996)[62] Waitlist control (20) Group-baseed CBT (20)	NR	NR
Hesser et al. (2012)[51] Control (online discussion forum) (32) Internet-based CBT (32)	NR	NR
Jasper et al.(2014)[49] Conrad et al. (2015)[193] Discussion forum control (44) Group-based CBT (43) Internet-based CBT (41)	NR	NR

Authors (Year) Interventions (N Randomized)	Safety Outcomes	Cost Outcomes
Kaldo et al. (2007)[55] Waitlist control (38) Book-guided CBT (34)	NR	NR
Kroner-Herwig et al. (2003)[59] Waitlist control (20) Group-based and Individual-based CBT (43)	NR	NR
Malouff et al. (2010)[52] Waitlist control (78) Book-guided CBT (84)	NR	NR
Martz et al. (2018)[61] Waitlist control group (10) Group-based CBT (10)	No adverse events (e.g., suicidal thinking) were reported during group sessions	NR
Nyenhuis et al. (2013)[50] Information-only control (77) Book-guided CBT (77) Internet-based CBT (79) Group-based CBT (71)	NR	NR
Robinson et al. (2008)[53] Waitlist control (27) Group-based CBT (38)	NR	NR
Sadlier et al. (2008)[56] Waitlist control (11) Indivdiual-based CBT (14)	NR	NR
Weise et al. (2016)[48] Discussion forum control (62) Internet-based CBT (62)	NR	NR
Weise et al. (2008)[54] Waitlist control (67) Individual-based CBT (63)	Adverse Effects Subscale Mean (SD): 1.5 (0.6); Range: 1 to 6; Indicating a majority of patients did not experience negative treatment side effects	NR
Zachriat et al. (2004)[58] Education-only (active control) (23) Group-based CBT (29) Tinnitus retraining therapy (31)	NR	NR
Zenner et al. (2013)[65] Waitlist control (120) Individual-based CBT (166)	40 adverse events reported (but not by group). Only 1 was considered treatment-related (Perception of "unpleasant images"). The other adverse events were upper respiratory infections, allergies, eczema, accidents, depression, sudden hearing loss.	NR

Abbreviations: CBT = cognitive behavioral therapy; NR = not reported; SD = standard deviation.

Table D4a. Study Characteristics for Included Tinnitus-Specific Interventions

Authors (Year)	Study Design	Sponsor	Country	Eligible Study Arms	Total N Overall/ Total N in Eligible Study Arms	Risk of Bias
Bauer et al. (2017)[73]	RCT	The Tinnitus Research Consortium	U.S.	Standard care Tinnitus retraining therapy	39/ 39	Some concerns
Caffier et al. (2006)[72]	RCT	NR	Germany	Waitlist control Tinnitus retraining therapy	48/ 48	High
Cima et al. (2012)[68] Maes et al. (2014)[194]	RCT	Netherlands Organization for Health Research and Development	The Netherlands	Usual care Tinnitus retraining therapy including cognitive behavioral therapy	492/ 492	Some concerns
Davis et al. (2008)[24]	RCT	Neuromonics Pty. Ltd.	Australia	Counseling only Neuromonics	69/ 69	High
Henry et al. (2016)[67]	RCT	Veterans Affairs Rehabilitation Research and Development and Veterans Health Administration	U.S.	Waitlist control Tinnitus education (active control) Tinnitus retraining therapy Tinnitus masking	148/ 148	Some concerns
Henry et al. (2007)[71]	RCT	VA Rehabilitation Research and Development Service; Veterans Health Administration	U.S.	No treatment Traditional support (attention control) Tinnitus retraining therapy	269/ 269	High
Krick et al. (2015)[74]	RCT	KTS Klaus Tschira Stiftung gGmbH (German nonprofit)	Germany	Waitlist control Music therapy	72/ 50	High
Seydel et al. (2010)[70]	RCT	NR	Germany	Waitlist control Tinnitus retraining therapy	237 enrolled, but only 90 randomized/ 90	High
Westin et al. (2011)[69]	RCT	Medical Research Council of Southeast Sweden, Swedish Council for Working Life and Social Research, masking devices provided at discounted rate by Starkey and GN Resound	Sweden	Waitlist control Tinnitus retraining therapy	42/ 64	Some concerns
Zachriat et al. (2004)[58]	RCT	Geers Foundation grant, noise generators donated by Hansaton, batteries donated by Energizer, sound generators fitted by Reuters Acoustics	Germany	Education only (active control) Cognitive behavioral therapy	77/ 77	High

Abbreviations: NR = not reported. RCT = randomized controlled trial; U.S. = United States; VA = Veterans Affairs.

Table D4b. Populations Characteristics of Included Tinnitus-specific Interventions

Authors (Year)	Study Population	Mean Age (SD)	N (% Female)	N (%) Race/Ethnicity	Other Characteristics
Bauer et al. (2017)[73]	Adults aged 18 to 75 years with chronic, bothersome tinnitus for more than 1 year recruited by print, radio, and internet ads *Inclusion:* Moderate to severe tinnitus defined as an average of 2 THI scores > 36 and difference between scores <17, non-pulsatile and continuous tinnitus, sensorineural hearing loss with subjective impairment, and symmetric sensorineural hearing loss amenable to amplification within limits of ReSound combination device. *Exclusion:* Medically or surgically treatable tinnitus, prior tinnitus treatment, Beck Depression Inventory > 30, reporting suicidal or self-harm on Beck Depression Inventory, current use of hearing aids	N (%) in age categories 18 to 50: 6 (16)* 51 to 65: 25 (66)* 66 to 75: 7 (18)*	12 (32)*	White: 38 (100)*	*Tinnitus Duration* N (%) in categories of tinnitus duration 1 to 2 years: 2(5)* 2 to 3 years: 4 (11)* 3 to 5 years: 3 (8)* More than 5 years: 29 (76)* *Hearing Loss* Hearing loss was an explicit inclusion criterion
Caffier et al. (2006)[72]	Adults with tinnitus for more than 6 months recruited from a tinnitus treatment center. *Inclusion:* Age 18 to 80 years, tinnitus for more than 6 months, ability to complete questionnaires *Exclusion:* Meniere's disease, vestibular schwannoma	51 (NR)	22 (46*)	NR	*Tinnitus Duration* Mean duration: 6.8 years *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled
Cima(2012)[68] Maes(2014)[194]	Adults with tinnitus *Inclusion:* Read and write Dutch *Exclusion:* Health issues that restricted ability to participate in intervention, treated at study site within last 5 years, pathological changes requiring medical treatment	54.2 (11.5)	184 (37)*	NR	*Tinnitus Duration* <1 y: 147 (30) 1 to 5 y: 191 (39) > 5y: 153 (31) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled
Davis et al. (2008)[24]	Adults with bothersome tinnitus *Inclusion:* Tinnitus-related disturbance (> 17 on TRQ), ENT evaluation confirmed medical treatment for tinnitus was not feasible *Exclusion:* Significant hearing loss, clinically significant mental health condition, continued	49.8 (15.8)	24 (48.0*)	NR	*Tinnitus Duration* Mean (SD) in years: 3.6 (4.1) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled

Authors (Year)	Study Population	Mean Age (SD)	N (% Female)	N (%) Race/Ethnicity	Other Characteristics
	exposure to conditions that could aggravate tinnitus, concurrent treatment including recent onset of hearing aid use or treatment that exceeded 1 hour per day, ongoing monetary compensation claims related to tinnitus				
Henry et al. (2016)[67]	Veterans with moderate to severe tinnitus recruited by direct VA referral, flyers at VA facilities, and newspaper ads *Inclusion:* Agreement between audiologist and participant that treatment would be worth potential benefits based on tinnitus-impact screening interview, moderate to severe tinnitus based on responses to 2 questions from the tinnitus severity index *Exclusion:* Positive screen for dementia (Blessed Orientation-Memory Concentration test score >10), psychological disorder that would not interfere with ability to serve as a participant in the study	61.7 (9.8)	4 (2.7)*	American Indian or Alaskan Native: 3 (2.0) Asian or Pacific Islander: 3 (2.0) Non-Hispanic Black: 4 (2.7) Hispanic: 6 (4.1) Non-Hispanic White: 128 (86.5) Other race/ethnicity: 4 (2.7)	*Tinnitus Duration* NR *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled
Henry et al. (2007)[71]	Veterans with clinically significant tinnitus recruited from VA medical centers and local newspaper and radio advertisements *Inclusion:* Sufficiently bothersome tinnitus, willing and able to complete study requirements including attending study information session *Exclusion:* NR	61.6 (9.9)	9 (3)	NR	*Tinnitus Duration* <1 yr: 9 (3*) 1–2 yr: 7 (3*) 3–5 yr: 21 (8*) 6–10 yr: 39 (14*) 10–20 yr: 62 (23*) >20 yr: 114 (42*) Unsure: 17 (6*) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled
Krick et al. (2015)[74]	Adults with tinnitus of less than 3 months that did not respond to initial medication management recruited from in a university ENT hospital	Control: 42.6 (11.5) Music: 43.9 (10.4)	PTC: 9# (41*) TG: 9# (45*)	NR	*Tinnitus Duration* Mean (SD) tinnitus duration in weeks Control: 8.1 (1.5) Music: 8.1 (1.9)

Authors (Year)	Study Population	Mean Age (SD)	N (% Female)	N (%) Race/Ethnicity	Other Characteristics
	Inclusion: Acute tinnitus persisting for maximum 3 months, without significant symptom change after initial medical intervention (glucocorticoids or rheological drugs) *Exclusion:* Tinnitus related to anatomic lesions of the inner ear, retrocochlear lesions, or cochlear implantation; diagnosis of a comorbid severe mental disorder, Meniere's Disease, or severe hyperacusis or hearing impairment more than 40 dB beyond the affected tinnitus frequencies		#f 42 partici-pants with baseline character-istics		*Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled *Other* N (%) with acoustic trauma Control: 7#(31,8*) Music: 8# (40*)
Seydel et al. (2010)[70]	Adults with tinnitus for at least 3 months referred by ENT specialists and psychologists to a tinnitus center *Inclusion:* Chronic tinnitus for at least 3 months; patients with profound hearing loss were only included if they were properly fit with hearing aids *Exclusion:* Very severe tinnitus-related distress, severe depression	51 (nr)	119 (50*)	NR	*Tinnitus Duration* N (%) with duration of tinnitus more than 10 years: 39 (18.8*) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled
Westin et al. (2011)[69]	Adults with tinnitus for at least 6 months recruited from audiology departments and newspaper ads *Inclusion:* Registered as regular patients of the public health care system; > = 18 years old; ccore of greater than or equal to 30 on the THI, duration of tinnitus > = 6 months *Exclusion:* Severe psychiatric disorder, previous psychological or sound-generator tinnitus treatment, or imediate medical need, severe hearing loss that would preclude the use of a wearable sound generator	Control: 49.6 (11.9) TRT: 49.0 (14.5)	Control: 8 (36) TRT: 8 (40)	NR	*Tinnitus Duration* Mean (SD) in years Control: 7.1 (7.7) TRT: 9.2 (6.6) *Hearing Loss* Profound hearing loss that would preclude use of a sound generator device was excluded
Zachriat et al. (2004)[58]	Adults with tinnitus for 3 months or more and a tinnitus disability score > = 25 recruited by newspaper ads *Inclusion:* Tinnitus duration of at least 3	Control: 56.1 (10.6) CBT: 53.8 (11.8) TRT: 51.6 (11.0)	Control: 5 (26)* CBT: 11 (41)*	NR	*Tinnitus Duration* Tinnitus duration in months (SD) Control: 90.2 (79.0) CBT: 68.5 (61.9)

Authors (Year)	Study Population	Mean Age (SD)	N (% Female)	N (%) Race/Ethnicity	Other Characteristics
	months, hearing capacity sufficient for group communication, tinnitus questionnaire score > = 25, sufficient hearing capacity for communication within groups *Exclusion:* Treatable organic causes of tinnitus, Meniere disease, ongoing psychotherapy or masker treatment		TRT: 10 (33)*		TRT: 65.4 (64.3) *Hearing Loss* Hearing loss was not an inclusion criterion, but some persons with hearing loss were enrolled

Notes: *Indicates a calculated value. #Of the 42 participants with baseline characteristics
Abbreviations: CBT = cognitive behavioral therapy; ENT = ear, nose, and throat; NA = not applicable; NR = not reported; SD = standard deviation; THI = Tinnitus Handicap Inventory; TRQ = Tinnitus Reaction Questionnaire; TRT = tinnitus retraining therapy; y = year.

Table D4c. Intervention Characteristics of Included Tinnitus-specific Interventions

Authors (Year)	Duration of Intervention	Control Group (N Randomized or Enrolled)	Intervention Group(s) (N Randomized or Enrolled)	Fidelity
Bauer et al. (2017)[73]	18 months	**Standard care (19)** Three individual 1-hour aural rehabilitation sessions using a standard presentation on mechanisms of hearing, hearing health, coping and listening strategies. Fitted with binaural combination devices identical to TRT group but with sound-generating feature inactive.	**Tinnitus retraining therapy (20)** Three individual 1-hour counseling sessions on hearing mechanisms, theories and examples of how hearing loss and emotional reactions lead to bothersome tinnitus. Fitted with binaural combination devices identical to control group but with sound-masking feature active.	NR
Caffier et al. (2006)[72]	12 months	**Waitlist control (20 after post-randomization exclusions)** No treatment for 12 months and then TRT.	**Tinnitus retraining therapy (20 after post-randomization exclusions)** Counseling every 3 months, auditory training, and progressive muscle relaxation, psychosomatic and psychotherapeutic care if needed, and mandatory binaural tinnitus control instruments (sound generator/masker). Normal hearing patients given low-level broadband noise generators and hearing loss patients given hearing aids or combined devices to use for at least 6 hours per day.	NR
Cima(2012)[68] Maes(2014)[194]	8 months	**Usual care (247)** Diagnostic consult including prescription of hearing aid and/or sound masker if indicated, check-up at 8 weeks. Among those with severe tinnitus, followups with social worker within 4-6 weeks after 3-month assessment for up to 12 weeks.	**TRT+CBT (245)** Diagnostic consult including prescription of hearing aid and/or sound masker if indicated and individual tinnitus retraining counseling to provide information about tinnitus and hearing loss, introduce neurophysiological model, and share treatment rationale; check-up at 8 weeks and 2-hour tinnitus group education session with CBT framework including TRT therapy, extensive neurophysical model explanation, fear avoidance discussion, and group discussion. Among those with severe complaint, intake with clinical psychologist and group treatments depending on severity and hearing loss that included group CBT, psychoeducation, cognitive restructuring, exposure techniques, mindfulness, stress relief, attention redirecting techniques, movement therapy, and applied relaxation. If group treatment contraindicated, then 60-minute individual sessions per discipline for up to 12 weeks.	Randomly assessed 40 patients per arm, no significant between-group differences in protocol adherence and contamination (P<0.6079)
Davis et al. (2008)[24]	12 months	**Counseling only (13)** Individual counseling based on principles of CBT that explained cause of tinnitus and	**Neuromonics (22)** Fitted with acoustic stimulus device in the form of music, instructed to listen for at least 2 hours per day, when tinnitus	Mean (SD) hours of use per day Neuromonics: 1.8

Authors (Year)	Duration of Intervention	Control Group (N Randomized or Enrolled)	Intervention Group(s) (N Randomized or Enrolled)	Fidelity
		coping strategies (e.g., avoid silence, over protection, and loud noises). Received additional counseling time to equal amount of time with clinicians as intervention groups.	was most disturbing. 13 of 22 patients instructed to set device at level that just covered up tinnitus and 9 of 22 instructed to set volume to cover tinnitus for only half of the time spent wearing the device. Taught relaxation strategies facilitated by acoustic stimulus. Individual counseling based on principles of CBT that explained cause of tinnitus and coping strategies (e.g., avoid silence, over protection, and loud noises). **Sound + counseling (15)** Fitted with acoustic stimulus device that emulated output of broadband noise generator, instructed to listen for as long as possible and a minimum of 2 hours per day, when tinnitus was most disturbing, with volume set to the lowest level at which both acoustic stimulus and tinnitus could be heard. Individual counseling based on principles of CBT that explained cause of tinnitus and coping strategies (e.g., avoid silence, over protection, and loud noises).	(1.4) Sound + Counseling: 1.4 (1.1)
Henry et al. (2016)[67]	18 mos.	**Waitlist control (33)** Nothing for 6 months, then randomization to one of three delayed treatment arms.	**Tinnitus education (active control) (39)** This was an active control group comprised of nonspecific therapy of similar length to TM and TRT group, trial use of hearing aid or combination instrument encouraged if hearing loss consistent with hearing aid candidacy **Tinnitus retraining therapy (34)** Structured counseling to teach unique TRT concepts, ear-level sound generators (maskers) if normal hearing or mild hearing loss, fitted with combination sound generators and hearing aids if hearing thresholds consistent with hearing aid candidacy **Tinnitus masking (42)** Structured counseling to teach TM concepts, ear-level sound generators (maskers), hearing aids, or a combination depending on level of hearing loss and participant preference	NR
Henry et al. (2007)[71]	4 weeks	**No treatment (91)** Received no treatment.	**Traditional support (attention control) (84)** Four weekly 1.5-hour group discussion sessions that provided no education **Tinnitus retraining therapy (94)** Four weekly 1.5-hour group TRT counseling sessions led by an audiologist that provided detailed information about	NR

Authors (Year)	Duration of Intervention	Control Group (N Randomized or Enrolled)	Intervention Group(s) (N Randomized or Enrolled)	Fidelity
			hearing, tinnitus, coping strategies, sound maskers, and auditory processing. Note: it is unclear whether sound generators were actually provided to participants as part of the intervention.	
Krick et al. (2015)[74]	9 consecutive 50-minute sessions in 1 week	**Waitlist control (25)** No intervention during study period; intervention offered to participants at the end of the study.	**Music therapy (25)** Heidelberg music therapy model, which consisted of: integration of active and receptive techniques for processing sound; acoustic attention control by active participation (including vocal exercises during and between therapy sessions); improvement of acoustic perception by training on intonation and listening capacity in the range of the transposed tinnitus frequency; musically based relaxation and well-being training; and educational, individualized tinnitus counseling. Therapy was conducted by a team of two experts, typically one music therapist and one psychotherapist.	NR
Seydel et al. (2010)[70]	7 days for active intervention, booster counseling at follow-up exams at 3 and 6 months and 1 year.	**Waitlist control (45)** Patients randomized to waitlist and examined at baseline and 3 months, waiting period did not exceed 3 months.	**TRT (45)** Multimodal tinnitus therapy including progressive muscle relaxation, education on hearing physiology, daily acoustic therapy, daily group CBT, 2 to 3 individual psychological consults. Each daily session lasted about 1 hour.	NR
Westin et al. (2011)[69]	18 months	**Waitlist control (22)** Nothing for 10 weeks, then individual, self-help, or group CBT starting at 10 weeks	**TRT (20)** Initial 2.5 hour consultation including wearable sound generator fitting, retraining counseling, and introduction to sound therapy followed by a 30-minute follow-up phone session.	67% of TRT participants indicated that they were wearing their sound generators for 8 hours or more everyday.
Zachriat et al. (2004)[58]	CBT: 12 weeks TRT: 24 weeks	**Education only (active control) (23)** One education session on the physiology and psychology of tinnitus, comparable to first education session in CBT and TRT.	**Cognitive behavioral therapy (29)** Termed tinnitus coping training by study authors; participants educated and counseled on physiology and psychology of tinnitus, relaxation exercises, attention distraction strategies, CBT-based approaches to identify and modify cognitive and emotional responses to tinnitus, avoidance behavior, and	NR

Authors (Year)	Duration of Intervention	Control Group (N Randomized or Enrolled)	Intervention Group(s) (N Randomized or Enrolled)	Fidelity
			relapse coping. Consisted of 11 weekly group sessions (6-8 participants) each 90-120 minutes in length **Tinnitus retraining therapy (31)** Termed habituation training by study authors; participants received group-based counseling modeled on tinnitus retraining therapy; focused on physiological and psychological distress of tinnitus as well as peripheral and central neuronal mechanisms involved in tinnitus perception, also received wide-band sound generators adapted individually by audiologist. Participants instructed to use the generators at least 6 hours per day. Five sessions total, each session held every 4 to 6 weeks over a total span of 6 months.	

Abbreviations: CBT = cognitive behavioral therapy; TM = tinnitus masking; TRT = tinnitus retraining therapy.

Table D4d. Efficacy Outcomes for Included Tinnitus-specific Interventions

Authors (Year) Interventions (N Randomized)	Name of Efficacy Measure	Results
Bauer et al. (2017)[73] Standard care (19) Tinnitus retraining therapy (20)	Tinnitus Handicap Inventory Yes	Between-group difference in change in score At 6 mos.: -6.8*, *P* >0.05 At 12 mos.: -9.5*, *P* < 0.05 At 18 mos.: -13.5*, *P* < 0.05 N (%) with 50% or better decrease in THI at 6 mos Control: 5 (26) TRT: 7 (37) *P* = 0.511* RD*: 10.5% (95% CI, -18.8 to 39.9) RR*: 1.4 (95% CI, 0.54 to 3.6) N (%) with 50% or better decrease in THI at 12 m Control: 6 (32) TRT: 13 (68) *P* = 0.029* RD*: 36.8% (95% CI, 7.3% to 66.4%) RR*: 2.2 (95% CI, 1.04 to 4.5) N (%) with 50% or better decrease in THI at 18 m Control: 7 (19) TRT: 14 (74) *P* = 0.028* RD*: 36.8% (95% CI, 7.5 to 66.2) RR*: 2.0 (95% CI, 1.05 to 3.8)
	Tinnitus Experience Questionnaire No	Loudness Between-group difference in change in score At 6 mos.: 3.2*, *P* >0.05 At 12 mos.: -8.5*, *P* > 0.05 At 18 mos.: -7.1*, *P* > 0.05 Effort to Ignore At 6 months: -11.3*, *P* < 0.05 At 12 months: -13.0*, *P* < 0.05 At 18 months: -8.6*, *P* <0.05
	Tinnitus Functional Index No	Between-group difference in change in score At 6 mos.: -3.1*, *P* > 0.05 At 12 mos.: -11.2*, *P* < 0.05 At 18 mos.: -9.6*, *P* <0.05

Authors (Year) Interventions (N Randomized)	Name of Efficacy Measure	Results
	Tinnitus Interview Questionnaire No	Rated negative impact Between-group difference in change in score At 6 mos.: -7.3*, *P* > 0.05 At 12 mos.: -8.4*, *P* > 0.05 At 18 mos.: -15.9*, *P* > 0.05 Percent of time aware Between-group difference in change in score At 6 mos.: -20.5*, *P* <0.05 At 12 mos.: -21.7*, *P* <0.05 At 18 mos.: -13.3*, *P* >0.05 Percent of time annoyed or distressed Between-group difference in change in score At 6 mos.: -25.7*, *P* > 0.05 At 12 mos.: -30.3*, *P* > 0.05 At 18 mos.: -25.1*, *P* > 0.05 TIQ Rated annoyance Between-group difference in change in score At 6 mos.: -23.0*, *P* > 0.05 At 12 mos.: -28.5*, *P* > 0.05 At 18 mos.: -27.6*, *P* > 0.05
Caffier et al. (2006)[72] Waitlist control (20after post-randomization exclusions) Tinnitus retraining therapy (20* after post-randomization exclusions)	Tinnitus Questionnaire Yes	At 12 mos. Between-group difference: NR, *P*<0.001
Cima et al. (2012)[68] Maes et al. (2014)[194] Usual care (247) TRT+CBT (245)	Tinnitus Handicap Inventory Yes	Adjusted mean between-group difference in change in score; *P* value; effect size At 3 mos.: -4.3 (95% CI, -7.1to -1.4); .0031; 0 .32 At 8 mos.: -7.6 (95% CI, -10.7 to -4.5); <0.0001; 0.52 At 12 mos.: -7.5 (95% CI, -10.7 to -4.4); <0.0001; ES = 0.45
	Tinnitus Questionnaire Yes	Adjusted mean between-group difference in change in score; *P* value; effect size At 3 mos.: -3.3 (95% CI, -5.6 to -1.0); .0048 ; 0.20 At 8 mos.: -7.1 (95% CI, -9.6 to -4.6); <0.0001; 0.41 At 12 mos.: -8.1 (95% CI, -10.8 to -5.3); <0.0001.; 0.43
	Hospital Anxiety and Depression Scale-	Adjusted mean between-group difference in change in score; *P* value; effect size At 3 mos.: -.86 (99% CI, -2.2 to 0.47); .0941 ; 0.15

Authors (Year) Interventions (N Randomized)	Name of Efficacy Measure	Results
	Depression No	At 8 mos.: -2.1 (99% CI, -3.5 to -0.66); 0.0002; 0.35 At 12 mos.: -1.5 (99% CI, -2.9 to -0.15); 0.0043 ; 0.24
	Health Utilities Index Yes	Adjusted mean between-group difference in change in score; *P* value; effect size At 3 mos.: -0.01 (95% CI,- 0.06 to 0.04); .6420; 0.04 At 8 mos.: 0.04 (95% CI, 0.01 to 0.07); .0258; 0.18 At 12 mos.: 0.06 (95% CI, 0.03 to 0.09); 0.0009; 0.24
	Tinnitus Catastrophising Scale No	Adjusted mean between-group difference in change in score; *P* value; effect size At 3 mos.: -2.1 (99% CI, -4.0 to -0.25); 0.0035; 031 At 8 mos.: -4.7 (99% CI, -6.9 to -2.4); 0.0001; 060 At 12 mos.: -3.8 (99% CI, -6.2 to -1.5); <0.0001.; 0.41
	Tinnitus-Related Fear Index No	Adjusted mean between-group difference in change in score; *P* value; effect size At 3 mos.: -0.79 (99% CI, -1.5 to -0.08); .0039; 0.35 At 8 mos.: -1.6 (99% CI, -2.4 to -0.75); <0.0001; 0.58 At 12 mos.: -1.5 (99% CI, -2.3 to -0.69); <0.001.; 0.48
Davis et al. (2008)[24] Counseling only (13) Neuromonics (22) Sound + counseling (15)	Tinnitus Reaction Questionnaire Yes	Repeated measures over 6-months followup Neuromonics had lower mean score compared to control according to figures in publication, but actual values and statistical significance testing NR Sound + counseling had similar scores compared with control; *P* NS Repeated measures over 12-months followup Neuromonics had significantly lower scores compared to control; actual values NR; *P* = 0.014 Sound + counseling had similar scores compared with control; *P* = 0.606 % with score < 17 at 6 months Control: 31 Neuromonics: 64; *P* = 0.07 vs. control (RD* 33.3% (95% CI, 1.2% to 65.43%; RR* 2.1 [95% CI, 0.87 to 5.0]) Sound + Counseling: 33; *P* = 0.91 vs. control (RD*2.3% [95% CI, -32.2% to 36.9%]; RR 1.1 [95% CI, 0.36 to 3.2])
	VAS for tinnitus loudness No	Repeated measures over 12 months Neuromonics had significantly lower scores compared with control; *P* < .001 Sound + counseling had similar scores compared with control; *P* = 0.091
	VAS for tinnitus severity No	Repeated measures over 12 months Neuromonics had significantly lower scores compared with control; *P* < .001 Sound+ counseling had similar scores compared with control; *P* = 0.884
	VAS for general relaxation level No	Repeated measures over 12 months Neuromonics had significantly lower scores compared to control; *P* = 0.003 Sound + counseling had similar scores compared with control; *P* = 0.696
Henry et al. (2016)[67] Waitlist control (33) Tinnitus education (active	Tinnitus Handicap Inventory Yes	Baseline Mean (SD), N Control: 47.5(24.2), 33 TED (active control): 49.5 (23.1), 39

Authors (Year) Interventions (N Randomized)	Name of Efficacy Measure	Results
control) (39) Tinnitus retraining therapy (34) Tinnitus masking (42)		TM: 52.6(21.3), 42 TRT: 49.2 (24.9), 34 3-mos. followup TM vs control Mean (SE) between-group difference: -11.0 (3.3) 95% CI: -17.6 to -4.4 *P* = 0.001 Effect size d = 0.44 TRT vs. control Mean (SE) between-group difference: -13.0 (3.5) 95% CI: -20.0 to -6.1 *P* <0.001 Effect size d = 0.52 TM vs TED (active control) Mean (SE) between-group difference: -4.14 (3.2) 95% CI: -10.5 to 2.2 *P* = 0.197 Effect size d = 0.16 TRT vs TED (active control) Mean (SE) between-group difference: -6.2 (3.4) 95% CI: -12.9 to 0.5 *P* = 0.07 Effect size d = 0.24 6-mos. followup TM vs control Mean (SE) between-group difference: -13.0 (4.0) 95% CI: -21.0 to -5.0 *P* = 0.002 Effect size d = 0.52 TRT vs control Mean (SE) between-group difference: -14.2 (4.3) 95% CI: -22.6 to -5.7 *P* = 0.001 Effect size d = 0.56 TM vs TED (active control) Mean (SE) between-group difference: -2.8 (3.9) 95% CI: -10.5 to 4.8

Authors (Year) Interventions (N Randomized)	Name of Efficacy Measure	Results
		P = 0.469 Effect size d = 0.11 TRT vs TED (active control) Mean between-group difference: -3.9 (4.1) 95% CI: -12.0 to 4.1 *P* = 0.336 Effect size d = 0.16 18 mos. followup TM vs TED (active control) Mean (SE) between-group difference: -2.9 (4.5) 95% CI:-11.7 to 5.9 *P* = 0.518 Effect size d = 0.11 TRT vs TED (active control) Mean (SE) between-group difference: -5.5 (4.7) 95% CI: -14.9 to 3.8 *P* = 0.242 Effect size d = 0.22 % with strong improvement by 6 mo. (score decrease of 20 points or more) Control: 3.0 TED (active control): 17.9 TM: 21.4 TRT: 20.6 % with modest improvement by 6 mo. (score at 3 mos or 6 mos was at least 7 to 19 points decreased) Control: 18.2 TED (active control): 25.6 TM: 21.4 TRT: 23.5 % with no change by 6 mo. (scores 3 mos. and 6 mos. were 6 points or less increased or decreased) Control: 42.4 TED (active control): 25.6 TM: 16.7 TRT: 23.5 % with moderate worsening by 6 mo. (scores at both 3 mos. and 6 mos. were increased by 7 points or more) Control: 21.2 TED (active control): 15.4 TM: 7.1

Authors (Year) Interventions (N Randomized)	Name of Efficacy Measure	Results
		TRT: 2.9 % with serious worsening by 6 mo.(scores at 3 mos. and 6 mos. were 20 points increased) Control: 15.2 TED (active control): 7.7 TM: 2.4 TRT: 2.9
Henry et al. (2007)[71] No treatment (91) Traditional support (attention control) (84) Tinnitus retraining therapy (94)	Tinnitus Severity Index Yes	TRT vs attention control Mean between-group difference in change in score At 6 mos.: -0.6* ; *P* = 0.47 At 12 mos.: -0.3*; *P* = 0.033 TRT vs no treatment control Mean between-group difference in change in score At 6 mos.: -3.3* ; *P* = 0.001 At 12 mos.: -2.4*; *P* = 0.013
Krick et al. (2015)[74] Waitlist control (25) Music therapy (25)	Tinnitus Questionnaire Yes	Mean (SD) change in score after treatment PCT: -1.8 (NR) TG: -17.7 (13.6) Between-group difference: 16; *P* unclear
Seydel et al. (2010)[70] Waitlist control (45) TRT (45)	Tinnitus Questionnaire No	Mean (SD) change in score at 3 mo Depicted on graph, actual values NR, *P* reported as <0.0001 in text but <0.01 on graph, both favoring TRT
	ADS (Depression) No	Mean (SD) change in score at 3 mo. Depicted on graph, actual values NR; *P* unclear, reported as <0.05 favoring TRT in text, but not identified as statistically significant on the graph
	Perceived Stress Scale No	Mean (SD) change at 3 mo. Depicted on graph, actual values NR; *P* reported as not significant (= .05) in text, not indicated as significant on graph
Westin et al. (2011)[69] Waitlist control (22) TRT (20)	Tinnitus Handicap Inventory Yes	Mean (SD) score at baseline; N Control: 49.3 (17.4), 22 TRT: 47.0 (18.2), 20 Mean (SD) score at 10 w, N Control: 48.3 (21.0), 22 TRT: 43.2(20.8), 20 Between-group difference: -5.1 (95% CI, -18.1 to 8.0); *P* = 0.44 Between-group difference adjusted for baseline differences*:-2.8
	Tinnitus Acceptance Questionnaire No	Mean (SD) score at baseline; N Control: 36.7(12.4), 22 TRT: 36.7 (10.0), 20

Authors (Year) Interventions (N Randomized)	Name of Efficacy Measure	Results
		Mean (SD) score at 10 w, N Control: 38.2 (11.2), 22 TRT: 37.9 (10.7), 20 Between-group difference*: -0.3 (95% CI, -7.2 to 6.6); *P* = 0.93 Between-group difference: adjusted for base
	Hospital Anxiety and Depression Scale-Depression No	Mean (SD) score at baseline; N Control: 6.4 (4.8), 22 TRT: 5.8 (3.8), 20 Mean (SD) score at 10 w, N Control: 6.2 (5.1), 22 TRT: 5.8 (3.7), 20 Between-group difference*: -0.42 (95% CI, -3.2 to 2.4), *P* = 0.77 Between-group difference adjusted for baseline
	Hospital Anxiety and Depression Scale-Anxiety No	Mean (SD) score at baseline; N Control: 7.6 (5.6), 22 TRT: 8.2 (3.8), 20 Mean (SD) score at 10 w , N Control: 7.2 (5.6), 22 TRT: 7.0 (4.2), 20 Between-group difference*: -0.2 (95% CI, -3.3 to 2.9), *P* = 0.90 Between-group difference adjusted for differences in baseline values*: -0.8
	Insomnia Severity Index No	Mean (SD) at baseline; N Control: 11.9 (6.6), 22 TRT: 12.6 (5.7) Mean (SD) at 10 w , N Control: 11.8 (6.1), 22 TRT: 13.1 (5.6),20 Between-group difference*: 1.3 (95% CI, -2.4 to 4.9), *P* = 0.49 Between-group difference adjusted for baseline differences*: 0.
	Quality of Life Inventory No	Mean (SD) score at baseline; N Control: 1.8 (1.8), 22 TRT: 2.2 (1.4), 20 Between-group difference*: 0.5 (95% CI, -0.53 to 1.5), *P* = .35 Mean (SD) score at 10 w, N Control: 1.9 (1.8), 22 TRT: 2.5 (1.7), 20 Between-group difference*: 0.6 (95% CI, -0.5 to 1

Authors (Year) Interventions (N Randomized)	Name of Efficacy Measure	Results
Zachriat et al. (2004)[58] Education only (active control) (23) Cognitive behavioral therapy (29) Tinnitus retraining therapy (31)	Tinnitus Questionnaire Yes	Between-group difference in change in score at 15 weeks CBT: -9.5* (at end of intervention); *P* = 0.018; effect size (d) 0.81 TRT: -8.1* (after 4 of 5 sessions completed); *P* = 0.015; effect size (d) 0.67

Abbreviations: CBT = cognitive behavioral therapy; CI = confidence interval; ES = effect size; mos. = months; RD = risk difference; RR = relative risk; SD = standard deviation; SE = standard error; TED = tinnitus education; TM = tinnitus masking; TIQ = Tinnitus Interview Questionnaire; THI = Tinnitus Handicap Inventory; TRT = tinnitus retraining therapy; VAS = visual analog scale.

Table D4e. Safety and Cost Outcomes for Included Tinnitus-specific Interventions

Authors (Year) Interventions (N Randomized)	Safety Outcomes	Cost Outcomes
Bauer et al. (2017)[73] Standard care (19) Tinnitus retraining therapy (20)	NR	NR
Caffier et al. (2006)[72] Waitlist control (20 after post-randomization exclusions) Tinnitus retraining therapy (20 after post-randomization exclusions)	NR	NR
Cima et al. (2012)[68] Maes et al. (2014)[194] Usual care (247) TRT+CBT (245)	Authors reported that "Adverse events as a result of treatment or measurements did not occur."	Mean total health care costs per patient (in 2009 U.S.$) over duration of intervention Usual care: $3,875 Specialized care: $4,023 Difference in cost from health care perspective: $152 (95% CI, $-333 to $643) Cost per QALY gained from health care perspective: $10,456 (95% CI, NR) Given a willingness to pay threshold of $45,000, there is 68% probability that specialized care is cost-effective. Mean total societal costs per patient (in 2009 U.S.$) over duration of intervention Usual care: $7,027 Specialized care: $7,380 Difference in cost from societal perspective: $357 (95% CI, -$1,034 to $1,782) Cost per QALY gained from societal perspective: $24,580 (95% CI, NR) Given a willingness-to-pay threshold of $45,000, there is 58% probability that specialized care is cost-effective.
Davis et al. (2008)[24] Counseling only (13) Neuromonics (22) Sound + counseling(15)	NR	NR
Henry et al. (2016)[67] Waitlist control (33) Tinnitus education (active control) (39) Tinnitus retraining therapy (34) Tinnitus masking (42)	NR	NR
Henry et al. (2007)[71] No treatment (91) Traditional support (attention control) (84)	NR	NR

Authors (Year) Interventions (N Randomized)	Safety Outcomes	Cost Outcomes
Tinnitus retraining therapy (94)		
Krick et al. (2015)[74] Waitlist control (25) Music therapy (25)	NR	NR
Seydel et al. (2010)[70] Waitlist control (45) TRT (45)	NR	NR
Westin et al. (2011)[69] Waitlist control (22) TRT (20)	NR	NR
Zachriat et la. (2004)[58] Education only (active control) (23) Cognitive behavioral therapy (29) Tinnitus retraining therapy (31)	NR	NR

Abbreviations: CBT = cognitive behavioral therapy; CI = confidence interval; NR = not reported; QALY = quality-adjusted life year gained; TRT = tinnitus retraining therapy; U.S. = United States.

Appendix E. Excluded Articles

List of Exclusion Codes

X1: Non-English language

X2: Abstract only publication

X3: Ineligible population

X4: Ineligible intervention

X5: Ineligible comparator

X6: Ineligible outcome

X7: Ineligible study design

X8: Ineligible study design: systematic review

X9: Ineligible comparator: comparative effectiveness

X10: Ineligible intervention: non-rTMS non-invasive neuromodulation intervention

X11: Ineligible intervention: non-CBT psych/behavioral intervention

X12: Ineligible setting: country

- Aazh H, Moore BC, Lammaing K, Cropley M. Tinnitus and hyperacusis therapy in a U.K. National Health Service audiology department: Patients' evaluations of the effectiveness of treatments. *Int J Audiol.* 2016;55(9):514-522. PMID: 27195947. doi: 10.1080/14992027.2016.1178400. Exclude: X6
- Ahnblad P, Nordkvist A. A Randomized, Placebo-Controlled, Double-Blind, Parallel Groups Study Evaluating the Performance and Safety of a Steady State Coherent Biomodulator Patch in the Treatment of Subjective Tinnitus. *Int Tinnitus J.* 2017;21(2):157-167. PMID: 29336135. doi: 10.5935/0946-5448.20170028. Exclude: X10
- Andersson G, Edsjo L, Kaldo V, Westin V. Tinnitus and short-term serial recall in stable versus intermittent masking conditions. *Scand J Psychol.* 2009;50(5):517-522. PMID: 19778399. doi: 10.1111/j.1467-9450.2009.00752.x. Exclude:
- Argstatter H, Grapp M, Hutter E, Plinkert PK, Bolay HV. The effectiveness of neuro-music therapy according to the Heidelberg model compared to a single session of educational counseling as treatment for tinnitus: a controlled trial. *J Psychosom Res.* 2015;78(3):285-292. PMID: 25224125. doi: 10.1016/j.jpsychores.2014.08.012. Exclude: X9
- Arif M, Sadlier M, Rajenderkumar D, James J, Tahir T. A randomised controlled study of mindfulness meditation versus relaxation therapy in the management of tinnitus. *J Laryngol Otol.* 2017;131(6):501-507. PMID: 28357966. doi: 10.1017/s002221511700069x. Exclude: X11
- Attias J, Shemesh Z, Shoham C, Shahar A, Sohmer H. Efficacy of self-hypnosis for tinnitus relief. *Scand Audiol.* 1990;19(4):245-249. PMID: 2075417. Exclude: X11
- Aydin N, Searchfield GD. Changes in tinnitus and physiological biomarkers of stress in response to short-term broadband noise and

sounds of nature. *Complement Ther Med.* 2019;46:62-68. PMID. doi: 10.1016/j.ctim.2019.07.018. Exclude: X9

- Bilici S, Yigit O, Taskin U, Gor AP, Yilmaz ED. Medium-term results of combined treatment with transcranial magnetic stimulation and antidepressant drug for chronic tinnitus. *Eur Arch Otorhinolaryngol.* 2015;272(2):337-343. PMID: 24337899. doi: 10.1007/s00405-013-2851-z. Exclude: X12
- Carrick DG, Davies WM, Fielder CP, Bihari J. Low-powered ultrasound in the treatment of tinnitus: a pilot study. *Br J Audiol.* 1986;20(2):153-155. PMID: 3719163. Exclude: X4
- Choy DS, Lipman RA, Tassi GP. Worldwide experience with sequential phase-shift sound cancellation treatment of predominant tone tinnitus. *J Laryngol Otol.* 2010;124(4):366-369. PMID: 20067647. doi: 10.1017/s0022215109992167. Exclude: X6
- Cima R, Joore M, Maes I, et al. Cost-effectiveness of multidisciplinary management of Tinnitus at a specialized Tinnitus centre. *BMC Health Serv Res.* 2009;9:29. PMID: 19210767. doi: 10.1186/1472-6963-9-29. Exclude: X7
- Cima RFF, van Breukelen G, Vlaeyen JWS. Tinnitus-related fear: Mediating the effects of a cognitive behavioural specialised tinnitus treatment. *Hear Res.* 2018;358:86-97. PMID. doi: 10.1016/j.heares.2017.10.003. Exclude: X6
- Davies S, McKenna L, Hallam RS. Relaxation and cognitive therapy: A controlled trial in chronic tinnitus. *Psychology & Health.* 1995;10(2):129-143. PMID: 1995-34296-001. doi: 10.1080/08870449508401943. Exclude: X9
- De Ridder D, Vanneste S. EEG driven tDCS versus bifrontal tDCS for tinnitus. *Frontiers in Psychiatry.* 2012;3(SEP). PMID. doi: 10.3389/fpsyt.2012.00084. Exclude: X10
- Dobie RA, Hoberg KE, Rees TS. Electrical tinnitus suppression: a double-blind crossover study. *Otolaryngol Head Neck Surg.* 1986;95(3 Pt 1):319-323. PMID: 3108780. doi: 10.1177/01945998860953p110. Exclude: X6
- dos Santos GM, Bento RF, de Medeiros IR, Oiticcica J, da Silva EC, Penteado S. The influence of sound generator associated with conventional amplification for tinnitus control: randomized blind clinical trial. *Trends Hear.* 2014;18. PMID: 25073131. doi: 10.1177/2331216514542657. Exclude: X12
- Emmert K, Kopel R, Koush Y, et al. Continuous vs. intermittent neurofeedback to regulate auditory cortex activity of tinnitus patients using real-time fMRI - A pilot study. *Neuroimage Clin.* 2017;14:97-104. PMID: 28154796. doi: 10.1016/j.nicl.2016.12.023. Exclude: X10
- Engelhardt J, Dauman R, Arne P, et al. Effect of chronic cortical

stimulation on chronic severe tinnitus: a prospective randomized double-blind cross-over trial and long-term follow up. *Brain Stimul.* 2014;7(5):694-700. PMID: 25017670. doi: 10.1016/j.brs.2014.05.008. Exclude: X4

- Erlandsson S, Ringdahl A, Hutchins T, Carlsson SG. Treatment of tinnitus: a controlled comparison of masking and placebo. *Br J Audiol.* 1987;21(1):37-44. PMID: 3828583. Exclude: X6
- Folmer RL, Carroll JR. Long-term effectiveness of ear-level devices for tinnitus. *Otolaryngol Head Neck Surg.* 2006;134(1):132-137. PMID: 16399193. doi: 10.1016/j.otohns.2005.09.030. Exclude: X7
- Fregni F, Marcondes R, Boggio PS, et al. Transient tinnitus suppression induced by repetitive transcranial magnetic stimulation and transcranial direct current stimulation. *Eur J Neurol.* 2006;13(9):996-1001. PMID: 16930367. doi: 10.1111/j.1468-1331.2006.01414.x. Exclude: X12
- Garin P, Gilain C, Van Damme JP, et al. Short- and long-lasting tinnitus relief induced by transcranial direct current stimulation. *J Neurol.* 2011;258(11):1940-1948. PMID: 21509429. doi: 10.1007/s00415-011-6037-6. Exclude: X10
- Ghossaini SN, Spitzer JB, Mackins CC, Zschommler A, Diamond BE, Wazen JJ. High-frequency pulsed electromagnetic energy in tinnitus treatment. *Laryngoscope.* 2004;114(3):495-500. PMID: 15091224. doi: 10.1097/00005537-200403000-00020. Exclude: X10
- Goebel G, Rubler D, Hiller W, Heuser J, Fichter MM. Evaluation of tinnitus retraining therapy in comparison to cognitive therapy and broad-band noise generator therapy. *Laryngo-Rhino-Otologie.* 2000;79(Suppl 1):S88. PMID. Exclude: X2
- Goebel G, Rubler D, Stepputat F, Hiller W, Heuser J, Fichter MM. Controlled prospective study of tinnitus retraining therapy compared to tinnitus coping therapy and broad-band noise generator therapy. Paper presented at: Proceedings of the International Tinnitus Seminar1999. Exclude: X6
- Hatanaka A, Ariizumi Y, Kitamura K. Pros and cons of tinnitus retraining therapy. *Acta Otolaryngol.* 2008;128(4):365-368. PMID: 18368566. doi: 10.1080/00016480701730760. Exclude: X7
- Hazell JW, Wood SM, Cooper HR, et al. A clinical study of tinnitus maskers. *Br J Audiol.* 1985;19(2):65-146. PMID: 3896355. Exclude: X4
- Heinecke K, Weise C, Rief W. Psychophysiological effects of biofeedback treatment in tinnitus sufferers. *Br J Clin Psychol.* 2009;48(Pt 3):223-239. PMID: 19079954. doi: 10.1348/014466508x386207. Exclude: X6
- Henin S, Fein D, Smouha E, Parra LC. The Effects of Compensatory Auditory Stimulation and High-Definition Transcranial Direct Current Stimulation (HD-tDCS) on

Tinnitus Perception - A Randomized Pilot Study. *PLoS One.* 2016;11(11):e0166208. PMID: 27832140. doi: 10.1371/journal.pone.0166208. Exclude: X9

- Henry JA, Schechter MA, Zaugg TL, et al. Clinical trial to compare tinnitus masking and tinnitus retraining therapy. *Acta Otolaryngol Suppl.* 2006(556):64-69. PMID: 17114146. doi: 10.1080/03655230600895556. Exclude: X9
- Henry JA, Schechter MA, Zaugg TL, et al. Outcomes of clinical trial: tinnitus masking versus tinnitus retraining therapy. *J Am Acad Audiol.* 2006;17(2):104-132. PMID: 16640064. Exclude: X9
- Herraiz C, Diges I, Cobo P, Plaza G, Aparicio JM. Auditory discrimination therapy (ADT) for tinnitus managment: preliminary results. *Acta Otolaryngol Suppl.* 2006(556):80-83. PMID: 17114148. doi: 10.1080/03655230600895614. Exclude: X7
- Herraiz C, Hernandez FJ, Plaza G, de los Santos G. Long-term clinical trial of tinnitus retraining therapy. *Otolaryngol Head Neck Surg.* 2005;133(5):774-779. PMID: 16274808. doi: 10.1016/j.otohns.2005.07.006. Exclude: X7
- Hesser H, Pereswetoff-Morath CE, Andersson G. Consequences of controlling background sounds: the effect of experiential avoidance on tinnitus interference. *Rehabil Psychol.* 2009;54(4):381-389. PMID: 19929119. doi: 10.1037/a0017565. Exclude: X4
- Hesser H, Westin VZ, Andersson G. Acceptance as a mediator in internet-delivered acceptance and commitment therapy and cognitive behavior therapy for tinnitus. *J Behav Med.* 2014;37(4):756-767. PMID: 23881309. doi: 10.1007/s10865-013-9525-6. Exclude: X6
- Hyvarinen P, Makitie A, Aarnisalo AA. Self-Administered Domiciliary tDCS Treatment for Tinnitus: A Double-Blind Sham-Controlled Study. *PLoS One.* 2016;11(4):e0154286. PMID: 27124116. doi: 10.1371/journal.pone.0154286. Exclude: X10
- Ireland CE, Wilson PH, Tonkin JP, Platt-Hepworth S. An evaluation of relaxation training in the treatment of tinnitus. *Behav Res Ther.* 1985;23(4):423-430. PMID: 3896227. doi: 10.1016/0005-7967(85)90170-6. Exclude: X4
- Jakes SC, Hallam RS, Rachman S, Hinchcliffe R. The effects of reassurance, relaxation training and distraction on chronic tinnitus sufferers. *Behav Res Ther.* 1986;24(5):497-507. PMID: 3530238. doi: 10.1016/0005-7967(86)90029-x. Exclude: X11
- Jalilvand H, Pourbakht A, Haghani H. Hearing aid or tinnitus masker: which one is the best treatment for blast-induced tinnitus? The results of a long-term study on 974 patients. *Audiol Neurootol.* 2015;20(3):195-201. PMID: 25924663. doi: 10.1159/000377617. Exclude: X5

- Jasper K, Weise C, Conrad I, Andersson G, Hiller W, Kleinstäuber M. The working alliance in a randomized controlled trial comparing Internet-based self-help and face-to-face cognitive behavior therapy for chronic tinnitus. *Internet Interventions.* 2014;1(2):49-57. PMID. doi: 10.1016/j.invent.2014.04.002. Exclude: X6
- Kallogjeri D, Piccirillo JF, Spitznagel E, Jr., et al. Cognitive Training for Adults With Bothersome Tinnitus: A Randomized Clinical Trial. *JAMA Otolaryngol Head Neck Surg.* 2017;143(5):443-451. PMID: 28114646. doi: 10.1001/jamaoto.2016.3779. Exclude: X11
- Kapkin O, Satar B, Yetiser S. Transcutaneous electrical stimulation of subjective tinnitus. A placebo-controlled, randomized and comparative analysis. *ORL J Otorhinolaryngol Relat Spec.* 2008;70(3):156-161. PMID: 18401195. doi: 10.1159/000124288. Exclude: X4
- Khedr EM, Rothwell JC, Ahmed MA, El-Atar A. Effect of daily repetitive transcranial magnetic stimulation for treatment of tinnitus: comparison of different stimulus frequencies. *J Neurol Neurosurg Psychiatry.* 2008;79(2):212-215. PMID: 18202212. doi: 10.1136/jnnp.2007.127712. Exclude: X12
- Kreuzer PM, Goetz M, Holl M, et al. Mindfulness-and body-psychotherapy-based group treatment of chronic tinnitus: a randomized controlled pilot study. *BMC Complement Altern Med.* 2012;12:235. PMID: 23186556. doi: 10.1186/1472-6882-12-235. Exclude: X11
- Krick CM, Argstatter H, Grapp M, Plinkert PK, Reith W. Heidelberg Neuro-Music Therapy enhances task-negative activity in tinnitus patients. *Frontiers in Neuroscience.* 2017;11(JUL). PMID. doi: 10.3389/fnins.2017.00384. Exclude: X6
- Landgrebe M, Binder H, Koller M, et al. Design of a placebo-controlled, randomized study of the efficacy of repetitive transcranial magnetic stimulation for the treatment of chronic tinnitus. *BMC Psychiatry.* 2008;8:23. PMID: 18412944. doi: 10.1186/1471-244x-8-23. Exclude: X7
- Langguth B, Landgrebe M, Frank E, et al. Efficacy of different protocols of transcranial magnetic stimulation for the treatment of tinnitus: Pooled analysis of two randomized controlled studies. *World J Biol Psychiatry.* 2014;15(4):276-285. PMID: 22909265. doi: 10.3109/15622975.2012.708438. Exclude: X7
- Lee SK, Chung H, Chung JH, Yeo SG, Park MS, Byun JY. Effectiveness of transcutaneous electrical stimulation for chronic tinnitus. *Acta Otolaryngol.* 2014;134(2):159-167. PMID: 24215217. doi: 10.3109/00016489.2013.844854. Exclude: X10
- Lehner A, Schecklmann M, Greenlee MW, Rupprecht R, Langguth B. Triple-site rTMS for the treatment of

chronic tinnitus: a randomized controlled trial. *Sci Rep.* 2016;6:22302. PMID: 26927363. doi: 10.1038/srep22302. Exclude: X5

- Li J, Jin J, Xi S, et al. Clinical efficacy of cognitive behavioral therapy for chronic subjective tinnitus. *Am J Otolaryngol.* 2019;40(2):253-256. PMID: 30477911. doi: 10.1016/j.amjoto.2018.10.017. Exclude: X9
- Li L, Shi H, Wang M. A Pilot Randomized Controlled Trial of Transcutaneous Electrical Nerve Stimulation for Patients With Acute Tinnitus. *Medicine (Baltimore).* 2019;98(1):e13793. PMID: 30608390. doi: 10.1097/md.0000000000013793. Exclude: X10
- Lindberg P, Scott B, Melin L, Lyttkens L. The psychological treatment of tinnitus: an experimental evaluation. *Behav Res Ther.* 1989;27(6):593-603. PMID: 2692553. doi: 10.1016/0005-7967(89)90143-5. Exclude: X6
- Lipman RI, Lipman SP. Phase-shift treatment for predominant tone tinnitus. *Otolaryngol Head Neck Surg.* 2007;136(5):763-768. PMID: 17478212. doi: 10.1016/j.otohns.2006.10.046. Exclude: X7
- Lugli M, Romani R, Ponzi S, Bacciu S, Parmigiani S. The windowed sound therapy: a new empirical approach for an effectiv personalized treatment of tinnitus. *Int Tinnitus J.* 2009;15(1):51-61. PMID: 19842347. Exclude: X6
- Maes IH, Cima RF, Vlaeyen JW, Anteunis LJ, Joore MA. Tinnitus: a cost study. *Ear Hear.* 2013;34(4):508-514. PMID: 23411656. doi: 10.1097/AUD.0b013e31827d113a. Exclude: X6
- Maes IH, Joore MA, Cima RF, Vlaeyen JW, Anteunis LJ. Assessment of health state in patients with tinnitus: a comparison of the EQ-5D and HUI mark III. *Ear Hear.* 2011;32(4):428-435. PMID: 21221004. doi: 10.1097/AUD.0b013e3181fdf09f. Exclude: X4
- Mahboubi H, Haidar YM, Kiumehr S, Ziai K, Djalilian HR. Customized Versus Noncustomized Sound Therapy for Treatment of Tinnitus: A Randomized Crossover Clinical Trial. *Ann Otol Rhinol Laryngol.* 2017;126(10):681-687. PMID: 28831839. doi: 10.1177/0003489417725093. Exclude: X9
- Malinvaud D, Londero A, Niarra R, et al. Auditory and visual 3D virtual reality therapy as a new treatment for chronic subjective tinnitus: Results of a randomized controlled trial. *Hear Res.* 2016;333:127-135. PMID: 26773752. doi: 10.1016/j.heares.2015.12.023. Exclude: X6
- Marcondes RA, Sanchez TG, Kii MA, et al. Repetitive transcranial magnetic stimulation improve tinnitus in normal hearing patients: a double-blind controlled, clinical and neuroimaging outcome study. *Eur J Neurol.* 2010;17(1):38-44. PMID: 19614962. doi: 10.1111/j.1468-1331.2009.02730.x. Exclude: X12

- McKenna L, Marks EM, Hallsworth CA, Schaette R. Mindfulness-Based Cognitive Therapy as a Treatment for Chronic Tinnitus: A Randomized Controlled Trial. *Psychother Psychosom.* 2017;86(6):351-361. PMID: 29131084. doi: 10.1159/000478267. Exclude: X11
- Mehlum D, Grasel G, Fankhauser C. Prospective crossover evaluation of four methods of clinical management of tinnitus. *Otolaryngol Head Neck Surg.* 1984;92(4):448-453. PMID: 6435067. doi: 10.1177/019459988409200414. Exclude: X6
- Mei ZG, Yang SB, Cai SJ, et al. Treatment of tinnitus with electrical stimulation on acupoint in the distribution area of ear vagus nerve combining with sound masking: Randomized controlled trial. *World Journal of Acupuncture - Moxibustion.* 2014;24(2):30-35. PMID. doi: 10.1016/S1003-5257(14)60022-2. Exclude: X5
- Mielczarek M, Olszewski J. Direct current stimulation of the ear in tinnitus treatment: a double-blind placebo-controlled study. *Eur Arch Otorhinolaryngol.* 2014;271(6):1815-1822. PMID: 24337877. doi: 10.1007/s00405-013-2849-6. Exclude: X10
- Neff P, Michels J, Meyer M, Schecklmann M, Langguth B, Schlee W. 10 Hz amplitude modulated sounds induce short-term tinnitus suppression. *Frontiers in Aging Neuroscience.* 2017;9(MAY). PMID. doi: 10.3389/fnagi.2017.00130. Exclude: X5
- Newman CW, Sandridge SA. A comparison of benefit and economic value between two sound therapy tinnitus management options. *J Am Acad Audiol.* 2012;23(2):126-138. PMID: 22353681. doi: 10.3766/jaaa.23.2.7. Exclude: X9
- Noh TS, Kyong JS, Chang MY, et al. Comparison of Treatment Outcomes Following Either Prefrontal Cortical-only or Dual-site Repetitive Transcranial Magnetic Stimulation in Chronic Tinnitus Patients: A Double-blind Randomized Study. *Otol Neurotol.* 2017;38(2):296-303. PMID: 28068305. doi: 10.1097/mao.0000000000001266. Exclude: X9
- Nyenhuis N, Zastrutzki S, Jager B, Kroner-Herwig B. An internet-based cognitive-behavioural training for acute tinnitus: secondary analysis of acceptance in terms of satisfaction, trial attrition and non-usage attrition. *Cogn Behav Ther.* 2013;42(2):139-145. PMID: 23205617. doi: 10.1080/16506073.2012.724081. Exclude: X6
- Onishi ET, Fukuda Y, Suzuki FA. Distortion product otoacoustic emissions in tinnitus patients. *Int Tinnitus J.* 2004;10(1):13-16. PMID: 15379342. Exclude: X4
- Ozimek E, Wicher A, Szyfter W, Szymiec E. Distortion product otoacoustic emission (DPOAE) in tinnitus patients. *J Acoust Soc Am.* 2006;119(1):527-538. PMID: 16454306. doi: 10.1121/1.2141297. Exclude: X4
- Pal N, Maire R, Stephan MA, Herrmann FR, Benninger DH. Transcranial Direct Current

Stimulation for the Treatment of Chronic Tinnitus: A Randomized Controlled Study. *Brain Stimul.* 2015;8(6):1101-1107. PMID: 26198363. doi: 10.1016/j.brs.2015.06.014. Exclude: X10

- Pantev C, Rudack C, Stein A, et al. Study protocol: Munster tinnitus randomized controlled clinical trial-2013 based on tailor-made notched music training (TMNMT). *BMC Neurol.* 2014;14:40. PMID: 24581050. doi: 10.1186/1471-2377-14-40. Exclude: X6

- Parazzini M, Del Bo L, Jastreboff M, Tognola G, Ravazzani P. Open ear hearing aids in tinnitus therapy: An efficacy comparison with sound generators. *Int J Audiol.* 2011;50(8):548-553. PMID: 21595527. doi: 10.3109/14992027.2011.572263. Exclude: X5

- Philippot P, Nef F, Clauw L, de Romree M, Segal Z. A randomized controlled trial of mindfulness-based cognitive therapy for treating tinnitus. *Clin Psychol Psychother.* 2012;19(5):411-419. PMID: 21567655. doi: 10.1002/cpp.756. Exclude: X11

- Podoshin L, Ben-David Y, Fradis M, Gerstel R, Felner H. Idiopathic subjective tinnitus treated by biofeedback, acupuncture and drug therapy. *Ear Nose Throat J.* 1991;70(5):284-289. PMID: 1914952. Exclude: X11

- Rheker J, Andersson G, Weise C. The role of "on demand" therapist guidance vs. no support in the treatment of tinnitus via the internet: A randomized controlled trial. *Internet Interventions.* 2015;2(2):189-199. PMID. doi: 10.1016/j.invent.2015.03.007. Exclude: X5

- Rief W, Weise C, Kley N, Martin A. Psychophysiologic treatment of chronic tinnitus: a randomized clinical trial. *Psychosom Med.* 2005;67(5):833-838. PMID: 16204446. doi: 10.1097/01.psy.0000174174.38908.c6. Exclude: X11

- Rikkert M, van Rood Y, de Roos C, Ratter J, van den Hout M. A trauma-focused approach for patients with tinnitus: The effectiveness of eye movement desensitization and reprocessing—A multicentre pilot trial. *European Journal of Psychotraumatology.* 2018;9(1). PMID: 2018-46309-001. doi: 10.1080/20008198.2018.1512248. Exclude: X11

- Roland LT, Peelle JE, Kallogjeri D, Nicklaus J, Piccirillo JF. The effect of noninvasive brain stimulation on neural connectivity in Tinnitus: A randomized trial. *Laryngoscope.* 2016;126(5):1201-1206. PMID: 26422238. doi: 10.1002/lary.25650. Exclude: X6

- Roland NJ, Hughes JB, Daley MB, Cook JA, Jones AS, McCormick MS. Electromagnetic stimulation as a treatment of tinnitus: a pilot study. *Clin Otolaryngol Allied Sci.* 1993;18(4):278-281. PMID: 8877185. Exclude: X6

- Schraven SP, Plontke SK, Rahne T, Wasserka B, Plewnia C. Hearing safety of long-term treatment with theta-burst stimulation. *Brain Stimul.*

2013;6(4):563-568. PMID: 23137700. doi: 10.1016/j.brs.2012.10.005. Exclude: X6

- Scott B, Lindberg P, Lyttkens L, Melin L. Psychological treatment of tinnitus. An experimental group study. *Scand Audiol.* 1985;14(4):223-230. PMID: 3912955. Exclude: X11
- Shabana MI, Dabbous AO, Abdelmajeed MA, Abdelkarim AMM. 'Counselling and amplification with and without fractal music (Zen tones) for management of patients suffering from hearing loss and tinnitus'. *Hearing, Balance and Communication.* 2018;16(1):41-55. PMID. doi: 10.1080/21695717.2017.1421812. Exclude: X12
- Shekhawat GS, Searchfield GD, Stinear CM. Randomized Trial of Transcranial Direct Current Stimulation and Hearing Aids for Tinnitus Management. *Neurorehabil Neural Repair.* 2014;28(5):410-419. PMID: 24213961. doi: 10.1177/1545968313508655. Exclude: X10
- Shekhawat GS, Vanneste S. High-definition transcranial direct current stimulation of the dorsolateral prefrontal cortex for tinnitus modulation: A preliminary trial. *Journal of Neural Transmission.* 2018;125(2):163-171. PMID: 2017-51169-001. doi: 10.1007/s00702-017-1808-6. Exclude: X10
- Simonetti P, Vasconcelos LG, Oiticica J. Effect of fractal tones on the improvement of tinnitus handicap inventory functional scores among chronic tinnitus patients: An open-label pilot study. *International Archives of Otorhinolaryngology.* 2018;22(4):387-394. PMID. doi: 10.1055/s-0038-1635575. Exclude: X5
- Smith JA, Mennemeier M, Bartel T, et al. Repetitive transcranial magnetic stimulation for tinnitus: a pilot study. *Laryngoscope.* 2007;117(3):529-534. PMID: 17334317. doi: 10.1097/MLG.0b013e31802f4154. Exclude: X6
- Steenerson RL, Cronin GW. Treatment of tinnitus with electrical stimulation. *Otolaryngol Head Neck Surg.* 1999;121(5):511-513. PMID: 10547461. doi: 10.1016/s0194-5998(99)70048-3. Exclude:
- Stephens SD, Corcoran AL. A controlled study of tinnitus masking. *Br J Audiol.* 1985;19(2):159-167. PMID: 3896354. Exclude: X4
- Stockdale D, McFerran D, Brazier P, et al. An economic evaluation of the healthcare cost of tinnitus management in the U.K. *BMC Health Serv Res.* 2017;17(1):577. PMID: 28830503. doi: 10.1186/s12913-017-2527-2. Exclude: X4
- Tass PA, Adamchic I, Freund HJ, von Stackelberg T, Hauptmann C. Counteracting tinnitus by acoustic coordinated reset neuromodulation. *Restor Neurol Neurosci.* 2012;30(2):137-159. PMID: 22414611. doi: 10.3233/rnn-2012-110218. Exclude: X10
- Thedinger BS, Karlsen E, Schack SH. Treatment of tinnitus with

electrical stimulation: an evaluation of the Audimax Theraband. *Laryngoscope.* 1987;97(1):33-37. PMID: 3491942. doi: 10.1288/00005537-198701000-00009. Exclude: X10

- Theodoroff SM, Griest SE, Folmer RL. Transcranial magnetic stimulation for tinnitus: using the Tinnitus Functional Index to predict benefit in a randomized controlled trial. *Trials.* 2017;18(1):64. PMID: 28183355. doi: 10.1186/s13063-017-1807-9. Exclude: X5

- Theodoroff SM, McMillan GP, Zaugg TL, Cheslock M, Roberts C, Henry JA. Randomized Controlled Trial of a Novel Device for Tinnitus Sound Therapy During Sleep. *Am J Audiol.* 2017;26(4):543-554. PMID: 29090311. doi: 10.1044/2017_aja-17-0022. Exclude: X9

- Thomas M, Laurell G, Lundeberg T. Vibratory stimulation as a treatment alternative in patients with tinnitus. *Ear Nose Throat J.* 1989;68(11):810-814, 817-818. PMID: 2693064. Exclude: X6

- To WT, Ost J, Hart J, Jr., De Ridder D, Vanneste S. The added value of auditory cortex transcranial random noise stimulation (tRNS) after bifrontal transcranial direct current stimulation (tDCS) for tinnitus. *J Neural Transm (Vienna).* 2017;124(1):79-88. PMID: 27761741. doi: 10.1007/s00702-016-1634-2. Exclude: X10

- Tugumia D, Samelli AG, Matas CG, Magliaro FC, Rabelo CM. Auditory training program in subjects with tinnitus. *Codas.* 2016;28(1):27-33. PMID: 27074186. doi: 10.1590/2317-1782/20162015113. Exclude: X12

- Tyler R, Cacace A, Stocking C, et al. Vagus Nerve Stimulation Paired with Tones for the Treatment of Tinnitus: A Prospective Randomized Double-blind Controlled Pilot Study in Humans. *Sci Rep.* 2017;7(1):11960. PMID: 28931943. doi: 10.1038/s41598-017-12178-w. Exclude: X4

- Tyler RS, Noble W, Coelho CB, Ji H. Tinnitus retraining therapy: mixing point and total masking are equally effective. *Ear Hear.* 2012;33(5):588-594. PMID: 22609540. doi: 10.1097/AUD.0b013e31824f2a6e. Exclude: X9

- Vanneste S, Fregni F, De Ridder D. Head-to-head comparison of transcranial random noise stimulation, transcranial AC stimulation, and transcranial DC stimulation for tinnitus. *Frontiers in Psychiatry.* 2013;4(DEC). PMID. doi: 10.3389/fpsyt.2013.00158. Exclude: X5

- Wang H, Li B, Feng Y, et al. A Pilot Study of EEG Source Analysis Based Repetitive Transcranial Magnetic Stimulation for the Treatment of Tinnitus. *PLoS One.* 2015;10(10):e0139622. PMID: 26430749. doi: 10.1371/journal.pone.0139622. Exclude: X12

- Wang H, Li B, Wang M, et al. Factor Analysis of Low-Frequency Repetitive Transcranial Magnetic Stimulation to the Temporoparietal Junction for Tinnitus. *Neural Plast.* 2016;2016:2814056. PMID:

27847647. doi: 10.1155/2016/2814056. Exclude: X5

- Wazen JJ, Daugherty J, Pinsky K, et al. Evaluation of a customized acoustical stimulus system in the treatment of chronic tinnitus. *Otol Neurotol.* 2011;32(4):710-716. PMID: 21451428. doi: 10.1097/MAO.0b013e318217d459. Exclude: X5
- Weber C, Arck P, Mazurek B, Klapp BF. Impact of a relaxation training on psychometric and immunologic parameters in tinnitus sufferers. *J Psychosom Res.* 2002;52(1):29-33. PMID: 11801262. doi: 10.1016/s0022-3999(01)00281-1. Exclude: X11
- White TP, Hoffman SR, Gale EN. Psychophysiological therapy for tinnitus. *Ear Hear.* 1986;7(6):397-399. PMID: 3539680. Exclude: X11
- Wise K, Rief W, Goebel G. Meeting the expectations of chronic tinnitus patients: comparison of a structured group therapy program for tinnitus management with a problem-solving group. *J Psychosom Res.* 1998;44(6):681-685. PMID: 9678749. doi: 10.1016/s0022-3999(97)00310-3. Exclude: X5
- Yadollahpour A, Mayo M, Saki N, Rashidi S, Bayat A. A chronic protocol of bilateral transcranial direct current stimulation over auditory cortex for tinnitus treatment: Dataset from a double-blinded randomized controlled trial. *F1000Res.* 2018;7:733. PMID: 30356442. doi: 10.12688/f1000research.14971.1. Exclude: X10
- Yakunina N, Kim SS, Nam EC. BOLD fMRI effects of transcutaneous vagus nerve stimulation in patients with chronic tinnitus. *PLoS One.* 2018;13(11):e0207281. PMID: 30485375. doi: 10.1371/journal.pone.0207281. Exclude: X6
- Zarenoe R, Hallgren M, Andersson G, Ledin T. Working Memory, Sleep, and Hearing Problems in Patients with Tinnitus and Hearing Loss Fitted with Hearing Aids. *J Am Acad Audiol.* 2017;28(2):141-151. PMID: 28240981. doi: 10.3766/jaaa.16023. Exclude:
- Zarenoe R, Soderlund LL, Andersson G, Ledin T. Motivational Interviewing as an Adjunct to Hearing Rehabilitation for Patients with Tinnitus: A Randomized Controlled Pilot Trial. *J Am Acad Audiol.* 2016;27(8):669-676. PMID: 27564444. doi: 10.3766/jaaa.15126. Exclude: X11
- Zhang M, Zhou H, Zhang J, Guo Y, Wang X, Wang N. [Evaluating the effects of hearing aids combined with psychological counseling on tinnitus in patients with deafness]. *Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi.* 2013;27(10):461-464. PMID: 23937007. Exclude: X4
- Zimmerman B, Finnegan M, Paul S, et al. Functional brain changes during mindfulness-based cognitive therapy associated with tinnitus severity. *Frontiers in Neuroscience.* 2019;13(JUL). PMID. doi: 10.3389/fnins.2019.00747. Exclude: X5

- Zöger S, Erlandsson S, Svedlund J, Holgers KM. Benefits from group psychotherapy in the treatment of severe refractory tinnitus. *Audiological Medicine.* 2008;6(1):62-72. PMID. doi: 10.1080/16513860801959092. Exclude: X5

Appendix F. Individual Study Risk of Bias Assessments

Table F1. Risk of Bias for Randomized Controlled Trials—Randomization Process F-2
Table F2. Risk of Bias for Randomized Controlled Trials—Deviations from Intended Interventions F-7
Table F3. Risk of Bias for Randomized Controlled Trials—Missing Outcome Data F-13
Table F4. Risk of Bias for Randomized Controlled Trials—Measurement of the Outcome F-17
Table F5. Risk of Bias for Randomized Controlled Trials—Selection of the Reported Result and Overall Risk of Bias Rating F-22

Table F1. Risk of Bias for Randomized Controlled Trials—Randomization Process

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Was the allocation sequence random?	Was allocation sequence concealed until participants were enrolled and assigned to interventions?	Did baseline differences between intervention groups suggest a problem with the randomization process?	Bias arising from the randomization process?	Comments
Abbott (2009)[64] CBT	PY	NI	PN	Some concerns	
Anders (2010)[26] rTMS	PY	NI	PY	High	Lower THI and TQ scores at baseline in sham group, no other baseline characteristics provided.
Andersson (2005)[57] CBT	PY	NI	Y	High	
Andersson (2002)[60] CBT	PY	PY	N	Low	
Barwood (2013)[27] rTMS	PY	NI	PY	High	Small sample size means baseline characteristics are probably not balanced.
Bauer (2017)[73] Tinnitus-Specific	Y	Y	N	Low	
Beukes (2018)[46] Beukes (2018)[192] CBT	Y	PY	N	Low	
Caffier (2006)[72] Tinnitus-Specific	PY	NI	NI	High	
Chung (2012)[28] rTMS	Y	NI	N	Some concerns	
Cima (2012)[68] Maes (2014)[194] Tinnitus-Specific	Y	Y	N	Low	
Davis (2008)[24] Sound & Tinnitus-Specific	N	N	NI	High	
Dineen (1999)[19] Dineen (1997)[190] Dineen (1997)[25] Sound	NI	NI	NI	High	
Folmer (2015)[29] rTMS	PY	PY	PY	Some concerns	There was a much higher proportion of participants with tinnitus duration > 20 years in the placebo group.
Formánek (2018)[30] rTMS	Y	NI	PN	Some concerns	rTMS group had shorter duration of tinnitus compared to sham, though could very well be due to chance

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Was the allocation sequence random?	Was allocation sequence concealed until participants were enrolled and assigned to interventions?	Did baseline differences between intervention groups suggest a problem with the randomization process?	Bias arising from the randomization process?	Comments
					given small numbers involved.
Henry (2019)[45] CBT	Y	Y	N	Low	
Henry (2017)[16] Sound	Y	Y	N	Low	
Henry (2017)[47] CBT	PY	Y	N	Low	
Henry (2016)[67] Tinnitus-Specific	PY	PY	N	Low	
Henry (2015)[189] Sound	NI	NI	PN	Some concerns	NI about randomization or allocation concealment
Henry (2007)[71] Tinnitus-Specific	Y	NI	N	Some concerns	
Henry (1998)[63] CBT	PY	NI	NI	High	
Henry (1996)[62] CBT	PY	NI	NI	High	
Hesser (2012)[51] CBT	Y	PY	N	Low	
Hiller (2005)[23] Sound	PY	NI	N	Some concerns	
Hoekstra (2013)[31] rTMS	Y	PY	PN	Low	
Jasper (2014)[49] Conrad (2015)[193] CBT	Y	PY	N	Low	
Kaldo (2007)[55] CBT	PY	NI	N	Some concerns	
Kleinjung (2005)[36] Langguth (2007)[191] rTMS	PY	NI	N	Some concerns	
Krick (2015)[74] Tinnitus-Specific	PY	NI	N	Some concerns	
Kroner-Herwig (2003)[59]	PY	PN	PY	Some concerns	Some imbalances in characteristics at baseline.

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Was the allocation sequence random?	Was allocation sequence concealed until participants were enrolled and assigned to interventions?	Did baseline differences between intervention groups suggest a problem with the randomization process?	Bias arising from the randomization process?	Comments
CBT					Method of randomization and allocation not robust.
Landgrebe (2017)[32] rTMS	Y	Y	N	Low	
Li (2016)[17] Sound	Y	PY	PN	Low	
Malouff (2010)[52] CBT	PY	N	NI	High	
Martz (2018)[61] CBT	Y	Y	NI	Some concerns	
Mennemeier (2011)[37] rTMS	PY	NI	NI	Some concerns	Method of randomization NR
Nyenhuis (2013)[50] CBT	Y	PY	N	Low	
Okamoto (2010)[22] Sound	N	N	NI	High	
Piccirillo (2013)[38] rTMS	Y	Y	NI	Low	
Piccirillo (2011)[39] rTMS	Y	PY	NI	Low	
Plewnia (2012)[33] rTMS	Y	Y	PN	Low	Age was higher in TAC group
Plewnia (2007)[40] rTMS	PY	NI	N	Some concerns	
Robinson (2008)[53] CBT	PY	NI	Y	High	
Rossi (2007)[41] rTMS	PY	NI	NI	Some concerns	Method of randomization not reported.
Sadlier (2008)[56] CBT	N	NI	PN	High	
Sahlsten (2017)[34] rTMS	PY	PY	N	Some concerns	
Schad (2018)[15] Sound	NI	NI	PY	High	Baseline scores higher in the notched group but adjusted for in the data analysis.
Schecklmann (2016)[35]	PY	NI	PN	Some concerns	

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Was the allocation sequence random?	Was allocation sequence concealed until participants were enrolled and assigned to interventions?	Did baseline differences between intervention groups suggest a problem with the randomization process?	Bias arising from the randomization process?	Comments
rTMS					
Seydel (2010)[70] Tinnitus-Specific	PN	NI	NI	High	No information about randomization, and while 237 were enrolled only 90 were randomized.
Stein (2016)[20] Sound	Y	PY	N	Low	
Strauss (2017)[21] Sound	Y	NI	NI	Some concerns	
Vanneste (2012)[42] rTMS	PY	N	NI	Some concerns	
Vanneste (2012)[43] rTMS	Y	NI	NI	Some concerns	
Vanneste (2011)[44] rTMS	N	NI	NI	High	
Weise (2016)[48] CBT	Y	NI	N	Some concerns	
Weise (2008)[54] CBT	Y	PY	N	Low	
Westin (2011)[69] Tinnitus-Specific	Y	PN	N	Some concerns	Some mention in the study that the allocation was not concealed by the study coordinator.
Wise (2016)[18] Sound	PY	NI	Y	High	Sample characteristics were only presented for study completers (N = 31); not for the participants randomized (N = 50). Serious imbalances in mean age (delta 10 years), duration of tinnitus (delta 11 years) level of hearing loss (delta 6), affective symptoms, and others.
Zachriat (2004)[58] CBT & Tinnitus-Specific	PY	PN	PY	High	Control group included participants with a much longer duration of tinnitus. Text in article suggests modification to a completely random process for allocation ("practical reasons led to the assignment of different numbers of patients to the groups; only 23 were assigned to education control because this number seemed sufficient to test the hypothesis."
Zenner (2013)[65] CBT	N	N	Y	High	

Abbreviations: CBT = cognitive behavioral therapy; N = No; NA = not applicable; NI = no information; NR = not reported; PN = probably no; PY = probably yes; RCT = randomized controlled trial; rTMS = repetitive transcranial magnetic stimulation; TAC = temporoparietal association cortex; THI = tinnitus handicap inventory; TQ = tinnitus questionnaire; Y = yes.

Table F2. Risk of Bias for Randomized Controlled Trials—Deviations from Intended Interventions

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Were participants aware of their assigned intervention during the trial?	Were carers and people delivering the interventions aware of participants' assigned intervention during the trials?	Were there deviations from the intended intervention that arose because of the trial context?	Were these deviations likely to have affected the outcome?	Were these deviations from intended intervention balanced between groups?	Was an appropriate analysis used to estimate the effect of assignment to intervention?	Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	Bias arising from deviations from intended interventions?	Comments
Abbott (2009)[64] CBT	Y	Y	PY	Y	N	Y	NA	High	
Anders (2010)[26] rTMS	N	Y	PN	NA	NA	Y	NA	Some concerns	
Andersson (2005)[57] CBT	Y	Y	PN	NA	NA	Y	NA	Some concerns	
Andersson (2002)[60] CBT	Y	Y	PY	PY	PN	Y	NA	Some concerns	
Barwood (2013)[27] rTMS	N	Y	PN	NA	NA	Y	NA	Some concerns	
Bauer (2017)[73] Tinnitus-Specific	Y	Y	N	NA	NA	Y	NA	Some concerns	
Beukes (2018)[46] Beukes (2018)[192] CBT	N	Y	PN	NA	NA	Y	NA	Some concerns	
Caffier (2006)[72] Tinnitus-Specific	Y	Y	PN	NA	NA	N	Y	High	Post-randomiza-tion exclusions
Chung (2012)[28] rTMS	N	NI	PN	NA	NA	Y	NA	Some concerns	
Cima (2012)[68] Maes (2014)[194] Tinnitus-Specific	N	PY	Y	Y	NI	Y	NA	Some concerns	
Davis (2008)[24] Sound & Tinnitus-Specific	Y	Y	Y	Y	NI	Y	NA	High	

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Were participants aware of their assigned intervention during the trial?	Were carers and people delivering the interventions aware of participants' assigned intervention during the trials?	Were there deviations from the intended intervention that arose because of the trial context?	Were these deviations likely to have affected the outcome?	Were these deviations from intended intervention balanced between groups?	Was an appropriate analysis used to estimate the effect of assignment to intervention?	Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	Bias arising from deviations from intended interventions?	Comments
Dineen (1999)[19] Dineen (1997)[190] Dineen (1997)[25] Sound	Y	Y	PN	NA	NA	Y	NA	Some concerns	
Folmer (2015)[29] rTMS	N	PN	NA	NA	NA	Y	NA	Some concerns	The principal investigator was aware, but the clinicians administer-ing the rTMS were not aware.
Formánek (2018)[30] rTMS	N	N	NA	NA	NA	Y	NA	Low	
Henry (2019)[45] CBT	Y	Y	N	NA	NA	Y	NA	Low	
Henry (2017)[16] Sound	Y	Y	N	NA	NA	Y	NA	Some concerns	
Henry (2017)[47] CBT	Y	Y	N	NA	NA	Y	NA	Some concerns	
Henry (2016)[67] Tinnitus-Specific	PY	PY	PN	NA	NA	Y	NA	Some concerns	
Henry (2015)[189] Sound	NI	NI	N	NA	NA	Y	NA	Some concerns	
Henry (2007)[71] Tinnitus-Specific	Y	Y	PN	NA	NA	Y	NA	Some concerns	
Henry (1998)[63] CBT	Y	Y	NI	NA	NA	PY	NA	Some concerns	

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Were participants aware of their assigned intervention during the trial?	Were carers and people delivering the interventions aware of participants' assigned intervention during the trials?	Were there deviations from the intended intervention that arose because of the trial context?	Were these deviations likely to have affected the outcome?	Were these deviations from intended intervention balanced between groups?	Was an appropriate analysis used to estimate the effect of assignment to intervention?	Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	Bias arising from deviations from intended interventions?	Comments
Henry (1996)[62] CBT	Y	Y	PN	NA	NA	Y	NA	Some concerns	
Hesser (2012)[51] CBT	Y	Y	N	NA	NA	Y	NA	Some concerns	
Hiller (2005)[23] Sound	Y	Y	N	NA	NA	Y	NA	Some concerns	
Hoekstra (2013)[31] rTMS	N	Y	PN	NA	NA	Y	NA	Some concerns	
Jasper (2014)[49] Conrad (2015)[193] CBT	Y	Y	PN	NA	NA	Y	NA	Some concerns	
Kaldo (2007)[55] CBT	Y	Y	PN	NA	NA	Y	NA	Some concerns	
Kleinjung (2005)[36] Langguth (2007)[191] rTMS	N	N	NA	NA	NA	Y	NA	Low	
Krick (2015)[74] Tinnitus-Specific	Y	Y	PN	NA	NA	Y	NA	Some concerns	
Kroner-Herwig (2003)[59] CBT	Y	Y	PN	NA	NA	Y	NA	Some concerns	
Landgrebe (2017)[32] rTMS	N	N	NA	NA	NA	Y	NA	Low	
Li (2016)[17] Sound	N	N	NA	NA	NA	Y	NA	Low	
Malouff (2010)[52] CBT	Y	Y	PN	NA	NA	N	Y	High	

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Were participants aware of their assigned intervention during the trial?	Were carers and people delivering the interventions aware of participants' assigned intervention during the trials?	Were there deviations from the intended intervention that arose because of the trial context?	Were these deviations likely to have affected the outcome?	Were these deviations from intended intervention balanced between groups?	Was an appropriate analysis used to estimate the effect of assignment to intervention?	Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	Bias arising from deviations from intended interventions?	Comments
Martz (2018)[61] CBT	Y	Y	Y	Y	N	Y	NA	High	
Mennemeier (2011)[37] rTMS	N	PN	NA	NA	NA	Y	NA	Low	
Nyenhuis (2013)[50] CBT	Y	Y	PN	NA	NA	Y	NA	Some concerns	
Okamoto (2010)[22] Sound	N	N	NA	NA	NA	PY	NA	Low	
Piccirillo (2013)[38] rTMS	N	N	NA	NA	NA	Y	NA	Low	
Piccirillo (2011)[39] rTMS	N	N	NA	NA	NA	Y	NA	Low	
Plewnia (2012)[33] rTMS	N	Y	PN	NA	NA	Y	NA	Some concerns	
Plewnia (2007)[40] rTMS	N	Y	PN	NA	NA	Y	NA	Some concerns	
Robinson (2008)[53] CBT	Y	Y	PN	NA	NA	Y	NA	Some concerns	
Rossi (2007)[41] rTMS	N	Y	PN	NA	NA	Y	NA	Some concerns	
Sadlier (2008)[56] CBT	Y	Y	PN	NA	NA	Y	NA	Some concerns	
Sahlsten (2017)[34] rTMS	N	Y	PN	NA	NA	Y	NA	Some concerns	
Schad (2018)[15] Sound	NI	NI	PN	NA	NA	Y	NA	Some concerns	

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Were participants aware of their assigned intervention during the trial?	Were carers and people delivering the interventions aware of participants' assigned intervention during the trials?	Were there deviations from the intended intervention that arose because of the trial context?	Were these deviations likely to have affected the outcome?	Were these deviations from intended intervention balanced between groups?	Was an appropriate analysis used to estimate the effect of assignment to intervention?	Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	Bias arising from deviations from intended interventions?	Comments
Schecklmann (2016)[35] rTMS	N	PY	PN	NA	NA	Y	NA	Some concerns	
Seydel (2010)[70] Tinnitus-Specific	Y	Y	N	NA	NA	Y	NA	Some concerns	
Stein (2016)[20] Sound	N	N	NA	NA	NA	Y	NA	Low	
Strauss (2017)[21] Sound	N	N	NA	NA	NA	Y	NA	Low	
Vanneste (2012)[42] rTMS	N	Y	PN	NA	NA	Y	NA	Some concerns	
Vanneste (2012)[43] rTMS	N	Y	PN	NA	NA	Y	NA	Some concerns	
Vanneste (2011)[44] rTMS	N	Y	PN	NA	NA	Y	NA	Some concerns	
Weise (2016)[48] CBT	Y	Y	PN	NA	NA	Y	NA	Some concerns	
Weise (2008)[54] CBT	Y	Y	PN	NA	NA	Y	NA	Some concerns	
Westin (2011)[69] Tinnitus-Specific	Y	Y	N	NA	NA	Y	NA	Low	
Wise (2016)[18] Sound	NI	NI	NI	NA	NA	Y	NA	Some concerns	
Zachriat (2004)[58] CBT & Tinnitus-Specific	Y	Y	NI	NA	NA	Y	NA	Some concerns	
Zenner (2013)[65] CBT	Y	Y	PN	NA	NA	Y	NA	Some concerns	

Abbreviations: CBT = cognitive behavioral therapy; N = No; NA = not applicable; NI = no information; PN = probably no; PY = probably yes; rTMS = repetitive transcranial magnetic stimulation; Y = yes.

Table F3. Risk of Bias for Randomized Controlled Trials—Missing Outcome Data

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Were data for this outcome available for all, or nearly all, participants randomized?	Is there evidence that the result was not biased by missing outcome data?	Could missingness in the outcome depend on its true value?	Is it likely that missingness in the outcome depended on its true value?	Bias arising from missing outcome data?	Comments
Abbott (2009)[64] CBT	Y	NA	NA	NA	Low	
Anders (2010)[26] rTMS	Y	NA	NA	NA	Low	
Andersson (2005)[57] CBT	Y	NA	NA	NA	Low	
Andersson (2002)[60] CBT	N	N	Y	PY	High	
Barwood (2013)[27] rTMS	Y	NA	NA	NA	Low	
Bauer (2017)[73] Tinnitus-Specific	Y	NA	NA	NA	Low	
Beukes (2018)[46] Beukes (2018)[192] CBT	Y	NA	NA	NA	Low	
Caffier (2006)[72] Tinnitus-Specific	PY	NA	NA	NA	Some concerns	
Chung (2012)[28] rTMS	PY	NA	NA	NA	Some concerns	No Consort
Cima (2012)[68] Maes (2014)[194] Tinnitus-Specific	Y	NA	NA	NA	Low	
Davis (2008)[24] Sound & Tinnitus-Specific	N	N	Y	Y	High	
Dineen (1999)[19] Dineen (1997)[190] Dineen (1997)[25] Sound	N	N	Y	Y	High	
Folmer (2015)[29] rTMS	Y	NA	NA	NA	Low	
Formánek (2018)[30] rTMS	Y	NA	NA	NA	Low	

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Were data for this outcome available for all, or nearly all, participants randomized?	Is there evidence that the result was not biased by missing outcome data?	Could missingness in the outcome depend on its true value?	Is it likely that missingness in the outcome depended on its true value?	Bias arising from missing outcome data?	Comments
Henry (2019)[45] CBT	PY	NA	NA	NA	Low	
Henry (2017)[16] Sound	Y	NA	NA	NA	Low	
Henry (2017)[47] CBT	N	PN	Y	Y	High	
Henry (2016)[67] Tinnitus-Specific	Y	NA	NA	NA	Low	
Henry (2015)[189] Sound	Y	NA	NA	NA	Low	
Henry (2007)[71] Tinnitus-Specific	N	N	Y	NI	High	> 20% attrition
Henry (1998)[63] CBT	NI	PN	PY	PY	High	
Henry (1996)[62] CBT	Y	NA	NA	NA	Low	
Hesser (2012)[51] CBT	Y	NA	NA	NA	Low	
Hiller (2005)[23] Sound	Y	NA	NA	NA	Low	
Hoekstra (2013)[31] rTMS	Y	NA	NA	NA	Low	
Jasper (2014)[49] Conrad (2015)[193] CBT	Y	NA	NA	NA	Low	
Kaldo (2007)[55] CBT	Y	NA	NA	NA	Low	
Kleinjung (2005)[36] Langguth (2007)[191] rTMS	PY	NA	NA	NA	Some concerns	
Krick (2015)[74] Tinnitus-Specific	Y	NA	NA	NA	Low	
Kroner-Herwig (2003)[59] CBT	N	N	Y	PY	High	High attrition and Differential attrition

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Were data for this outcome available for all, or nearly all, participants randomized?	Is there evidence that the result was not biased by missing outcome data?	Could missingness in the outcome depend on its true value?	Is it likely that missingness in the outcome depended on its true value?	Bias arising from missing outcome data?	Comments
Landgrebe (2017)[32] rTMS	Y	NA	NA	NA	Low	
Li (2016)[17] Sound	N	N	Y	NI	High	32% attrition
Malouff (2010)[52] CBT	N	N	Y	NI	High	>20% attrition
Martz (2018)[61] CBT	Y	NA	NA	NA	Low	
Mennemeier (2011)[37] rTMS	PY	NA	NA	NA	Some concerns	
Nyenhuis (2013)[50] CBT	Y	NA	NA	NA	Some concerns	
Okamoto (2010)[22] Sound	N	N	Y	Y	High	
Piccirillo (2013)[38] rTMS	Y	NA	NA	NA	Low	
Piccirillo (2011)[39] rTMS	Y	NA	NA	NA	Low	
Plewnia (2012)[33] rTMS	Y	NA	NA	NA	Low	
Plewnia (2007)[40] rTMS	PY	NA	NA	NA	Low	
Robinson (2008)[53] CBT	N				High	37% attrition
Rossi (2007)[41] rTMS	PY	NA	NA	NA	Some concerns	
Sadlier (2008)[56] CBT	Y	NA	NA	NA	Low	
Sahlsten (2017)[34] rTMS	Y	NA	NA	NA	Low	
Schad (2018)[15] Sound	Y	NA	NA	NA	Low	
Schecklmann (2016)[35] rTMS	Y	NA	NA	NA	Low	

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Were data for this outcome available for all, or nearly all, participants randomized?	Is there evidence that the result was not biased by missing outcome data?	Could missingness in the outcome depend on its true value?	Is it likely that missingness in the outcome depended on its true value?	Bias arising from missing outcome data?	Comments
Seydel (2010)[70] Tinnitus-Specific	NI	PN	PY	PY	Some concerns	
Stein (2016)[20] Sound	Y	NA	NA	NA	Low	For the immediate post-treatment measures, but not for the 3-month followup.
Strauss (2017)[21] Sound	Y	NA	NA	NA	Low	
Vanneste (2012)[42] rTMS	PY	NA	NA	NA	Some concerns	No Consort
Vanneste (2012)[43] rTMS	PY	NA	NA	NA	Some concerns	
Vanneste (2011)[44] rTMS	PY	NA	NA	NA	Some concerns	No Consort
Weise (2016)[48] CBT	Y	NA	NA	NA	Low	
Weise (2008)[54] CBT	Y	NA	NA	NA	Low	
Westin (2011)[69] Tinnitus-Specific	Y	NA	NA	NA	Low	
Wise (2016)[18] Sound	N	N	NI	NI	High	Only available for 62% of those randomized
Zachriat (2004)[58] CBT & Tinnitus-Specific	Y	NA	NA	NA	Low	
Zenner (2013)[65] CBT	Y	NA	NA	NA	Low	

Abbreviations: CBT = cognitive behavioral therapy; N = no; NA = not applicable; NI = no information; PN = probably no; PY = probably yes; rTMS = repetitive transcranial magnetic stimulation; Y = yes.

Table F4. Risk of Bias for Randomized Controlled Trials—Measurement of the Outcome

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Was the method of measuring the outcome appropriate?	Could measurement of ascertainment of the outcome have differed between intervention groups?	Were outcome assessors aware of the intervention received by study participants?	Could assessment of the outcome have been influenced by knowledge of intervention received?	Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	Bias arising from measurement of the outcome?	Comments
Abbott (2009)[64] CBT	Y	PN	NA	NA	NA	Some concerns	
Anders (2010)[26] rTMS	N	PN	PN	NA	NA	Low	
Andersson (2005)[57] CBT	N	PN	Y	PY	NI	Some concerns	
Andersson (2002)[60] CBT	N	PN	Y	PY	NI	Some concerns	
Barwood (2013)[27] rTMS	N	PN	PN	NA	NA	Low	
Bauer (2017)[73] Tinnitus-specific	N	PN	Y	Y	NI	Some concerns	
Beukes (2018)[46] Beukes (2018)[192] CBT	N	PN	PN	NA	NA	Low	
Caffier (2006)[72] Tinnitus-specific	N	PN	Y	PY	NI	Some concerns	
Chung (2012)[28] rTMS	N	PN	PN	NA	NA	Low	
Cima (2012)[68] Maes (2014)[194] Tinnitus-specific	N	PN	N	NA	NA	Low	
Davis (2008)[24] Sound & tinnitus-specific	N	N	Y	Y	Y	Some concerns	
Dineen (1999)[19] Dineen (1997)[190] Dineen (1997)[25] Sound	N	PN	Y	PY	PY	Some concerns	

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Was the method of measuring the outcome appropriate?	Could measurement of ascertainment of the outcome have differed between intervention groups?	Were outcome assessors aware of the intervention received by study participants?	Could assessment of the outcome have been influenced by knowledge of intervention received?	Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	Bias arising from measurement of the outcome?	Comments
Folmer (2015)[29] rTMS	N	N	N	NA	NA	Low	
Formánek (2018)[30] rTMS	PN	PN	N	NA	NA	Low	
Henry (2019)[45] CBT	PN	PN	PY	PY	PY	Some concerns	
Henry (2017)[16] Sound	N	N	Y	PY	PY	Some concerns	
Henry (2017)[47] CBT	N	N	Y	PY	PY	Some concerns	
Henry (2016)[67] Tinnitus-specific	N	PN	Y	PY	PY	Some concerns	
Henry (2015)[189] Sound	N	N	NI	NI	NI	Some concerns	
Henry (2007)[71] Tinnitus-specific	N	PN	Y	Y	NI	Some concerns	
Henry (1998)[63] CBT	N	PN	Y	PY	NI	Some concerns	
Henry (1996)[62] CBT	N	PN	Y	PY	NI	Some concerns	
Hesser (2012)[51] CBT	N	PN	NI	PY	PY	Some concerns	
Hiller (2005)[23] Sound	N	N	NI	PY	PY	Some concerns	
Hoekstra (2013)[31] rTMS	N	N	N	NA	NA	Low	
Jasper (2014)[49] Conrad (2015)[193] CBT	N	PN	Y	PY	NI	Some concerns	
Kaldo (2007)[55] CBT	N	N	Y	PY	NI	Some concerns	

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Was the method of measuring the outcome appropriate?	Could measurement of ascertainment of the outcome have differed between intervention groups?	Were outcome assessors aware of the intervention received by study participants?	Could assessment of the outcome have been influenced by knowledge of intervention received?	Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	Bias arising from measurement of the outcome?	Comments
Kleinjung (2005)[36] Langguth (2007)[191] rTMS	N	PN	PN	NA	NA	Low	
Krick (2015)[74] Tinnitus-specific	N	N	Y	PY	PY	Some concerns	
Kroner-Herwig (2003)[59] CBT	PN	PN	Y	Y	PY	Some concerns	
Landgrebe (2017)[32] rTMS	N	PN	N	NA	NA	Low	
Li (2016)[17] Sound	N	N	N	NA	NA	Low	
Malouff (2010)[52] CBT	PN	PN	Y	Y	NI	Some concerns	
Martz (2018)[61] CBT	N	PN	Y	PY	NI	Some concerns	
Mennemeier (2011)[37] rTMS	N	PN	PN	NA	NA	Low	
Nyenhuis (2013)[50] CBT	N	PN	Y	Y	PY	Some concerns	
Okamoto (2010)[22] Sound	PN	PN	PN	NA	NA	Low	
Piccirillo (2013)[38] rTMS	N	N	N	NA	NA	Low	
Piccirillo (2011)[39] rTMS	N	PN	PN	NA	NA	Low	
Plewnia (2012)[33] rTMS	N	PN	PN	NA	NA	Low	
Plewnia (2007)[40] rTMS	N	PN	PN	NA	NA	Low	
Robinson (2008)[53] CBT	N	PN	Y	PY	NI	Some concerns	

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Was the method of measuring the outcome appropriate?	Could measurement of ascertainment of the outcome have differed between intervention groups?	Were outcome assessors aware of the intervention received by study participants?	Could assessment of the outcome have been influenced by knowledge of intervention received?	Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	Bias arising from measurement of the outcome?	Comments
Rossi (2007)[41] rTMS	N	PN	PN	NA	NA	Low	
Sadlier (2008)[56] CBT	Y	PN	NA	NA	NA	High	HADS measures were collected retrospectively
Sahlsten (2017)[34] rTMS	N	N	N	NA	NA	Low	
Schad (2018)[15] Sound	N	PN	NI	PY	PY	Some concerns	
Schecklmann (2016)[35] rTMS	N	N	PN	NA	NA	Low	
Seydel (2010)[70] Tinnitus-specific	N	N	Y	PY	PY	High	
Stein (2016)[20] Sound	N	N	N	NA	NA	Low	
Strauss (2017)[21] Sound	PN	PN	PN	NA	NA	Low	
Vanneste (2012)[42] rTMS	N	N	PN	NA	NA	Low	
Vanneste (2012)[43] rTMS	N	PN	PN	NA	NA	Low	
Vanneste (2011)[44] rTMS	N	PN	PN	NA	NA	Low	
Weise (2016)[48] CBT	N	N	Y	PY	PY	Some concerns	
Weise (2008)[54] CBT	N	PN	Y	PY	NI	Some concerns	
Westin (2011)[69] Tinnitus-specific	N	N	Y	PY	NI	Some concerns	
Wise (2016)[18] Sound	N	N	NI	PY	NI	Some concerns	

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Was the method of measuring the outcome appropriate?	Could measurement of ascertainment of the outcome have differed between intervention groups?	Were outcome assessors aware of the intervention received by study participants?	Could assessment of the outcome have been influenced by knowledge of intervention received?	Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	Bias arising from measurement of the outcome?	Comments
Zachriat (2004)[58] CBT & Tinnitus-specific	N	Y	NA	NA	NA	High	Measurement of the outcome for the TRT group occurred before the end of the intervention.
Zenner (2013)[65] CBT	N	PN	Y	PY	NI	Some concerns	

Abbreviations: CBT = cognitive behavioral therapy; HADS = hospital anxiety and depression scale; N = no; NA = not applicable; NI = no information; PN = probably no; PY = probably yes; rTMS = repetitive transcranial magnetic stimulation; TRT = tinnitus retraining therapy; Y = yes.

Table F5. Risk of Bias for Randomized Controlled Trials—Selection of the Reported Result and Overall Risk of Bias Rating

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Were the data that produced this result analyzed in accordance with a prespecified analysis plan that was finalized before unblinded outcome data were available for analysis?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible outcome measurements within the same domain?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible analyses of the data?	Bias arising from selection of reported results?	Comments	Overall rating	Rationale/Comments
Abbott (2009)[64] CBT	NI	N	N	Some concerns		High	Unclear cluster randomization procedure; no information about allocation concealment, participants in intervention group had much high duration of tinnitus compared to control group; intervention not blinded, use of patient-reported outcomes means that outcome assessment was also not blinded; very poor adherence to the intervention in the treatment group, no prespecified analysis plan.
Anders (2010)[26] rTMS	NI	N	N	Some concerns		High	No information about method of randomization or allocation concealment combined with lower severity of tinnitus in sham group raises high risk for bias as no other data on baseline characteristics provided and not clear that these baseline differences were adjusted for in the analysis, investigators not blinded, no prespecified analysis plan.
Andersson (2005)[57] CBT	NI	N	N	Some concerns		High	No information about how participants were randomized, no information about allocation concealment, few baseline characteristics presented to assess adequacy of randomization, baseline scores on TRQ, anxiety, and depression measures suggest moderate imbalances in group at baseline. Intervention not blinded, use of patient-reported outcomes means that outcome assessment was also not blinded, no pre-specified analysis plan.

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Were the data that produced this result analyzed in accordance with a prespecified analysis plan that was finalized before unblinded outcome data were available for analysis?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible outcome measurements within the same domain?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible analyses of the data?	Bias arising from selection of reported results?	Comments	Overall rating	Rationale/Comments
Andersson (2002)[60] CBT	NI	N	N	Some concerns		High	Intervention was not blinded, use of patient-reported outcomes also means that outcome assessment was not blinded. High attrition, and at least one analysis demonstrates bias in outcome comparing true intent to treat vs. completers analysis. No prespecified analysis plan.
Barwood (2013)[27] rTMS	NI	N	N	Some concerns		High	No information about allocation concealment and small sample size results in differences in baseline characteristics. Investigators not blinded to treatment allocation, outcome assessors not blinded, no prespecified analysis plan.
Bauer (2017)[73] Tinnitus-specific	NI	N	N	Some concerns		Some concerns	Intervention was not blinded, use of patient-reported outcomes means that outcome assessment was also not blinded, no information about prespecified analysis plan.
Beukes (2018)[46] Beukes (2018)[192] CBT	NI	N	N	Some concerns		Some concerns	Investigators were not blinded to intervention; no prespecified analysis plan.
Caffier (2006)[72] Tinnitus-specific	NI	N	N	Some concerns		High	No information about method of randomization and no mention of allocation concealment, no baseline characteristics provided to assess adequacy of randomization, post-randomization exclusions for noncompliance and missing data and dropouts; intervention not blinded, use of patient-reported outcomes means that outcome assessment also not blinded. No pre-specified analysis plan.

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Were the data that produced this result analyzed in accordance with a prespecified analysis plan that was finalized before unblinded outcome data were available for analysis?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible outcome measurements within the same domain?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible analyses of the data?	Bias arising from selection of reported results?	Comments	Overall rating	Rationale/Comments
Chung (2012)[28] rTMS	NI	N	N	Some concerns		Some concerns	No information about method of randomization or allocation concealment, unclear whether investigators were blinded, no information about number of patients eligible/randomized vs. number analyzed, no prespecified analysis plan.
Cima (2012)[68] Maes (2014)[194] Tinnitus-specific	NI	N	N	Low		Some concerns	Participants received somewhat individualized interventions; all the components of each intervention were described per a protocol, but not all participants received every element of the protocol per design. Thus, the effect estimate represents the effect of individualizing treatment guided by a standard protocol, rather than the effect of a very proscribed intervention. Not clear that there was a prespecified analysis plan, though the trial was registered.
Davis (2008)[24] Sound & Tinnitus-specific	NI	PN	PN	Some concerns		High	Inadequate method of randomization and allocation concealment, no information about how baseline characteristics varied by group; interventions were not blinded, and because patient-reported outcomes were used, outcomes assessment was also not blinded. No prespecified analysis plan. Although 69 patients appeared to be eligible, only 50 were used for data analysis with 19 being excluded post-randomization.

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Were the data that produced this result analyzed in accordance with a prespecified analysis plan that was finalized before unblinded outcome data were available for analysis?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible outcome measurements within the same domain?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible analyses of the data?	Bias arising from selection of reported results?	Comments	Overall rating	Rationale/Comments
Dineen (1999)[19] Dineen (1997)[190] Dineen (1997)[25] Sound	NI	PN	PN	Some concerns		High	No information about randomization or allocation concealment and no baseline characteristics for the groups of interest; intervention was not blinded and used patient-reported outcomes which could be influenced by lack of blinding. No prespecified analysis plan, and high attrition (40%) by 12 months.
Folmer (2015)[29] rTMS	NI	N	N	Low		Some concerns	Groups were not balanced at baseline with respect to tinnitus duration and this was not adjusted for in the analysis. The principal investigator was not blinded to treatment assignment, though the clinicians and outcome assessors were blinded.
Formánek (2018)[30] rTMS	NI	PY	PN	Some concerns		Some concerns	No information about allocation concealment and baseline imbalance on tinnitus duration that might be due to small numbers enrolled; no prespecified analysis plan, and multiple tinnitus-specific measures employed.
Henry (2019)[45] CBT	NI	PY	PY	Some concerns		Some concerns	Intervention could not be blinded to participants or caregivers; due to the nature of the outcome assessments (patient-reported outcomes) the outcome assessment could also not be blinded. Multiple instruments used to assess effectiveness, though one was designated as the primary outcome measure.
Henry (2017)[16] Sound	NI	N	N	Some concerns		Some concerns	Interventions were not blinded; use of patient-reported outcomes also means that outcome assessors were not blinded. No prespecified analysis plan.

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Were the data that produced this result analyzed in accordance with a prespecified analysis plan that was finalized before unblinded outcome data were available for analysis?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible outcome measurements within the same domain?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible analyses of the data?	Bias arising from selection of reported results?	Comments	Overall rating	Rationale/Comments
Henry (2017)[47] CBT	NI	N	N	Some concerns		High	Intervention was not blinded to participants, caregivers, and use patient-reported outcomes means outcome assessment was also not blinded. > 20% of randomized participants did not have data at followup. No prespecified analysis plan.
Henry (2016)[67] Tinnitus-specific	NI	N	N	Some concerns		Some concerns	Interventions were not blinded to participants or caregivers, use of patient-reported outcomes also means outcome assessment was not blinded. No information about whether a prespecified analysis plan was used.
Henry (2015)[189] Sound	NI	PN	PN	Some concerns		Some concerns	No information about randomization or allocation concealment; unclear whether intervention was blinded and mostly used patient-reported outcomes which could be impacted by lack of participant blinding. No prespecified analysis plan.
Henry (2007)[71] Tinnitus-specific	NI	N	N	Some concerns		High	No information about allocation concealment, intervention was not blinded, use of patient-reported outcomes means that outcome assessment was also not blinded. High attrition (> 20%); no prespecified analysis plan.

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Were the data that produced this result analyzed in accordance with a prespecified analysis plan that was finalized before unblinded outcome data were available for analysis?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible outcome measurements within the same domain?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible analyses of the data?	Bias arising from selection of reported results?	Comments	Overall rating	Rationale/Comments
Henry (1998)[63] CBT	NI	PY	N	High		High	No information about method of randomization, no information about allocation concealment, baseline characteristics not provided by group to assess adequacy of randomization; intervention not blinded, use of patient-reported outcomes also means that outcome assessment not blinded; unclear how many participants were randomized and analyzed per group, unable to assess missing data by group, unclear whether participants that dropped were included in the analysis; no prespecified analysis plan; authors report on 7 tinnitus-specific measures.
Henry (1996)[62] CBT	NI	Y	N	High		High	No information about method of randomization or allocation concealment and no reporting of baseline characteristics by group to assess adequacy of randomization; intervention not blinded, use of patient-reported outcomes means that outcome assessment was also not blinded. Study reported multiple outcome measures in same domain (11 different tinnitus-specific measures); no prespecified analysis plan.
Hesser (2012)[51] CBT	NI	PN	PN	Some concerns		Some concerns	Intervention was not blinded to participants or caregivers, patient-reported outcomes were used and may be influenced by the fact that participants were not blinded. No prespecified analysis plan.

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Were the data that produced this result analyzed in accordance with a prespecified analysis plan that was finalized before unblinded outcome data were available for analysis?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible outcome measurements within the same domain?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible analyses of the data?	Bias arising from selection of reported results?	Comments	Overall rating	Rationale/Comments
Hiller (2005)[23] Sound	NI	N	N	Some concerns		Some concerns	No information about method of randomization and allocation concealment, intervention was not blinded to participants or caregivers, and because of use of patient-reported outcomes, outcome assessment was also no blinded. No information on whether a prespecified analysis plan was used.
Hoekstra (2013)[31] rTMS	NI	PN	PN	Some concerns		Some concerns	Clinicians were not blinded; no prespecified analysis plan.
Jasper (2014)[49] Conrad (2015)[193] CBT	NI	N	N	Some concerns		Some concerns	Intervention not blinded; use of patient-reported outcomes also means that outcome assessment was not blinded. No prespecified analysis plan.
Kaldo (2007)[55] CBT	NI	N	N	Some concerns		Some concerns	No information about allocation concealment and study was not blinded; use of patient-reported outcomes means that outcome assessment was also not blinded. No prespecified analysis plan.
Kleinjung (2005)[36] Langguth (2007)[191] rTMS	NI	N	N	Some concerns		Some concerns	No information about method of randomization or allocation concealment, no information about number of patients eligible/enrolled vs. number analyzed, no prespecified analysis plan.
Krick (2015)[74] Tinnitus-specific	NI	N	N	Some concerns		High	Some concerns for bias in nearly all domains, method of randomization and allocation concealment not reported, intervention not blinded and use of patient-reported outcome means that outcome assessors also not blinded, no prespecified analysis plan.

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Were the data that produced this result analyzed in accordance with a prespecified analysis plan that was finalized before unblinded outcome data were available for analysis?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible outcome measurements within the same domain?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible analyses of the data?	Bias arising from selection of reported results?	Comments	Overall rating	Rationale/Comments
Kroner-Herwig (2003)[59] CBT	NI	Y	N	High		High	Nonstandard method of randomization and allocation concealment, some evidence of imbalances at baseline, intervention not blinded, use of patient-reported outcomes means outcome assessment also not blinded, more than 20% attrition in treatment group, with evidence of differential attrition. Combination of outcomes into clusters for analysis obscures impact on individual validated outcome measures that were used. No prespecified analysis plan.
Landgrebe (2017)[32] rTMS	Y	N	N	Low		Low	No comments.
Li (2016)[17] Sound	NI	N	N	Some concerns		High	High attrition (32%) and post-randomization exclusions for noncompliance. No prespecified analysis plan.
Malouff (2010)[52] CBT	NI	PN	PN	Some concerns		High	Randomized by dice roll, so likely no allocation concealment. Intervention not blinded, and primary analysis was not intention to treat and had > 20% attrition. Patient-reported outcomes means that outcome assessment was also not blinded. No prespecified analysis plan.

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Were the data that produced this result analyzed in accordance with a prespecified analysis plan that was finalized before unblinded outcome data were available for analysis?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible outcome measurements within the same domain?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible analyses of the data?	Bias arising from selection of reported results?	Comments	Overall rating	Rationale/Comments
Martz (2018)[61] CBT	NI	N	N	Some concerns		High	No baseline characteristics provided to assess adequacy of randomization. Intervention was not blinded, and patient-reported outcomes used so outcome assessment also not blinded. Very poor fidelity to intervention, only 4 of the 10 participants allocated to the CBT intervention attended the sessions. No prespecified analysis plan.
Mennemeier (2011)[37] rTMS	NI	N	N	Some concerns		Some concerns	Method of randomization and allocation concealment was not reported, no information about number of patients eligible/enrolled vs. number analyzed, no prespecified analysis plan.
Nyenhuis (2013)[50] CBT	NI	N	N	Some concerns		Some concerns	Intervention not blinded, use of patient-reported outcomes also means that outcome assessment not blinded; although intent to treat analysis was used, authors had to impute data for the 39% of participants that dropped out after baseline. No prespecified analysis plan.

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Were the data that produced this result analyzed in accordance with a prespecified analysis plan that was finalized before unblinded outcome data were available for analysis?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible outcome measurements within the same domain?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible analyses of the data?	Bias arising from selection of reported results?	Comments	Overall rating	Rationale/Comments
Okamoto (2010)[22] Sound	NI	N	N	High	Statistical significance testing for months 1-6 for tinnitus loudness NR; high risk for selected outcomes reporting.	High	Study used “pseudorandomization" with no mention of allocation concealment and no presentation of baseline characteristics to assess adequacy of randomization. High attrition (~40%). High potential for selected outcomes reporting; significance testing only reported for tinnitus loudness for months 7 to 12, but not for months 1 to 6.
Piccirillo (2013)[38] rTMS	PY	N	N	Low		High	No information on baseline characteristics by group. Only 70% of the randomized participants completed the study per protocol; analysis was among only the 14 who completed the study. At least some of the participants withdrew due to reasons that may have influenced the outcome (e.g., insomnia). No prespecified analysis plan was mentioned.
Piccirillo (2011)[39] rTMS	PY	N	N	Low		Some concerns	Allocation concealment methods were not described. Baseline characteristics were not presented by group. No prespecified analysis plan was presented.
Plewnia (2012)[33] rTMS	NI	PN	PN	Some concerns		Some concerns	Investigators not blinded; no prespecified analysis plan.
Plewnia (2007)[40] rTMS	NI	N	N	Some concerns		Some concerns	No information about method of randomization or allocation concealment, investigators were not blinded, no prespecified analysis plan.

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Were the data that produced this result analyzed in accordance with a prespecified analysis plan that was finalized before unblinded outcome data were available for analysis?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible outcome measurements within the same domain?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible analyses of the data?	Bias arising from selection of reported results?	Comments	Overall rating	Rationale/Comments
Robinson (2008)[53] CBT	NI	Y	N	High		High	No information about method of randomization or allocation concealment; groups were not balanced at baseline with respect to tinnitus distress; intervention not blinded, use of patient-reported outcomes means outcome assessment also not blinded; 37% attrition; no prespecified analysis plan and used 6 different tinnitus-specific measures.
Rossi (2007)[41] rTMS	NI	N	N	Some concerns		Some concerns	Method of randomization and allocation concealment not reported, investigators were not blinded, no information about number eligible/enrolled vs. number analyzed, no prespecified analysis plan.
Sadlier (2008)[56] CBT	NI	N	N	Some concerns		High	Participants allocated consecutively not randomly and no information about allocation concealment. Intervention not blinded, use of patient-reported outcomes means that outcome assessment was also not blinded. Some baseline measures (specifically HADS) were assessed retrospectively after treatment completed. No prespecified analysis plan.
Sahlsten (2017)[34] rTMS	NI	N	N	Some concerns		Some concerns	No detail on method of randomization and allocation concealment; participants but not clinicians were blinded, no prespecified analysis plan.

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Were the data that produced this result analyzed in accordance with a prespecified analysis plan that was finalized before unblinded outcome data were available for analysis?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible outcome measurements within the same domain?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible analyses of the data?	Bias arising from selection of reported results?	Comments	Overall rating	Rationale/Comments
Schad (2018)[15] Sound	NI	N	N	Some concerns		High	No information about randomization or allocation concealment and evidence that groups were not balanced at baseline, although the analysis did account for that. No information about blinding of intervention to participants, clinicians, or outcome assessors, no prespecified analysis plan.
Schecklmann (2016)[35] rTMS	NI	N	N	Some concerns		Some concerns	No information about method of randomization or allocation concealment; patients were blinded but not the clinicians. No prespecified analysis plan.
Seydel (2010)[70] Tinnitus-specific	NI	N	N	Some concerns		High	Although 237 enrolled, only 90 were randomized, no information about randomization or allocation concealment and no baseline characteristics by group provided. Intervention was not blinded to participants or caregivers, patient-reported outcomes were used and may be influenced by the fact that participants were not blinded.
Stein (2016)[20] Sound	PY	PN	PN	Low		Some concerns	Investigators only analyzed treatment completers; discontinuation was due to adverse effects, perceived quality of the music, and too time consuming.

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Were the data that produced this result analyzed in accordance with a prespecified analysis plan that was finalized before unblinded outcome data were available for analysis?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible outcome measurements within the same domain?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible analyses of the data?	Bias arising from selection of reported results?	Comments	Overall rating	Rationale/Comments
Strauss (2017)[21] Sound	NI	N	N	Some concerns		Some concerns	Very little information about baseline characteristics provided to assess adequacy of randomization, not enough information reported for the single outcome reported to assess adequacy of analysis. Data is only reported on a figure, with no mention of whether statistical significance testing performed and no data to assess precision provided.
Vanneste (2012)[42] rTMS	NI	N	N	Some concerns		High	No information about randomization or allocation concealment or baseline characteristics between-groups, intervention not blinded to investigators, no information about how many patients eligible/randomized vs. analyzed; no prespecified analysis plan.
Vanneste (2012)[43] rTMS	NI	N	N	Some concerns		Some concerns	No information about allocation concealment, intervention not blinded to investigators, no information about number eligible/randomized vs. number analyzed, no prespecified analysis plan.
Vanneste (2011)[44] rTMS	NI	N	N	Some concerns		High	In this crossover trial, the order of active vs. sham was not randomized, investigators were not blinded to treatment assignment, no information about number of participants enrolled/eligible vs. number analyzed; no prespecified analysis plan.

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Were the data that produced this result analyzed in accordance with a prespecified analysis plan that was finalized before unblinded outcome data were available for analysis?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible outcome measurements within the same domain?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible analyses of the data?	Bias arising from selection of reported results?	Comments	Overall rating	Rationale/Comments
Weise (2016)[48] CBT	NI	N	N	Some concerns		Some concerns	No information about allocation concealment, intervention not blinded, use of patient-reported outcomes also means outcome assessors not blinded, no information about prespecified analysis plan.
Weise (2008)[54] CBT	NI	N	N	Some concerns		Some concerns	Intervention not blinded, use of patient-reported outcomes means outcomes assessment was also not blinded. No prespecified analysis plan.
Westin (2011)[69] Tinnitus-Specific	NI	N	N	Low		Some concerns	Unclear allocation concealment, lack of prespecified analysis plan, participants and clinicians were not blinded, outcome assessment was mostly patient-reported outcomes which could be influenced by lack of blinding.
Wise (2016)[18] Sound	NI	N	N	Some concerns		High	Minimal information about randomization and allocation concealment and no information about baseline characteristics for the entire randomized population; baseline characteristics of study completers were not balanced at baseline suggesting selection bias related to non-random attrition. Further, overall attrition was high, only 62% of participants randomized completed the study. No information about blinding; given the nature of the intervention, it is likely participants (and thus outcome assessors) were not blinded. No prespecified analysis plan.

Main Study Author (Year); Companion Studies Author (Year) Intervention Type	Were the data that produced this result analyzed in accordance with a prespecified analysis plan that was finalized before unblinded outcome data were available for analysis?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible outcome measurements within the same domain?	Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible analyses of the data?	Bias arising from selection of reported results?	Comments	Overall rating	Rationale/Comments
Zachriat (2004)[58] CBT & tinnitus-specific	NI	N	N	Some concerns		High	Dice were used for randomization with some unspecified modifications that resulted in lower number of participants in control group; no information about allocation concealment. Interventions were not blinded; measurement of the outcome in the TRT arm occurred prior to the end of the intervention. No prespecified analysis plan.
Zenner (2013)[65] CBT	NI	N	N	Some concerns		High	Quasi-experimental design, participants not randomized but rather received intervention based on which clinic they were enrolled at. Intervention was not blinded, use of patient-reported outcomes means that outcome assessors were also not blinded. No prespecified analysis plan.

Abbreviations: CBT = cognitive behavioral therapy; HADS = hospital anxiety and depression scale; N = no; NA = not applicable; NI = no information; NR = not reported; PN = probably no; PY = probably yes; rTMS = repetitive transcranial magnetic stimulation; TRT = tinnitus retraining therapy; TRQ = tinnitus reaction questionnaire; Y = yes.

Appendix G. Studies Using Comparative Effectiveness, Neuromodulation, or Psychological Therapies Outside the Scope of This Review

Comparative effectiveness studies excluded at full text review

- Argstatter H, Grapp M, Hutter E, Plinkert PK, Bolay HV. The effectiveness of neuro-music therapy according to the Heidelberg model compared to a single session of educational counseling as treatment for tinnitus: a controlled trial. Journal of psychosomatic research. 2015 Mar;78(3):285-92.
- Aydin N, Searchfield GD. Changes in tinnitus and physiological biomarkers of stress in response to short-term broadband noise and sounds of nature. Complement Ther Med. 2019;46:62-8.
- Davies S, McKenna L, Hallam RS. Relaxation and cognitive therapy: A controlled trial in chronic tinnitus. Psychology & Health. 1995;10(2):129-43.
- Henin S, Fein D, Smouha E, Parra LC. The Effects of Compensatory Auditory Stimulation and High-Definition Transcranial Direct Current Stimulation (HD-tDCS) on Tinnitus Perception - A Randomized Pilot Study. PloS one. 2016;11(11):e0166208.
- Henry JA, Schechter MA, Zaugg TL, Griest S, Jastreboff PJ, Vernon JA, et al. Clinical trial to compare tinnitus masking and tinnitus retraining therapy. Acta oto-laryngologica Supplementum. 2006 Dec(556):64-9.
- Henry JA, Schechter MA, Zaugg TL, Griest S, Jastreboff PJ, Vernon JA, et al. Outcomes of clinical trial: tinnitus masking versus tinnitus retraining therapy. Journal of the American Academy of Audiology. 2006 Feb;17(2):104-32.
- Li J, Jin J, Xi S, Zhu Q, Chen Y, Huang M, et al. Clinical efficacy of cognitive behavioral therapy for chronic subjective tinnitus. American journal of otolaryngology. 2019 Mar - Apr;40(2):253-6.
- Mahboubi H, Haidar YM, Kiumehr S, Ziai K, Djalilian HR. Customized Versus Noncustomized Sound Therapy for Treatment of Tinnitus: A Randomized Crossover Clinical Trial. The Annals of otology, rhinology, and laryngology. 2017 Oct;126(10):681-7.
- Newman CW, Sandridge SA. A comparison of benefit and economic value between two sound therapy tinnitus management options. Journal of the American Academy of Audiology. 2012 Feb;23(2):126-38.
- Noh TS, Kyong JS, Chang MY, Park MK, Lee JH, Oh SH, et al. Comparison of Treatment Outcomes Following Either Prefrontal Cortical-only or Dual-site Repetitive Transcranial Magnetic Stimulation in Chronic Tinnitus Patients: A Double-blind Randomized Study. Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology. 2017 Feb;38(2):296-303.

- Theodoroff SM, McMillan GP, Zaugg TL, Cheslock M, Roberts C, Henry JA. Randomized Controlled Trial of a Novel Device for Tinnitus Sound Therapy During Sleep. American journal of audiology. 2017 Dec 12;26(4):543-54.
- Tyler RS, Noble W, Coelho CB, Ji H. Tinnitus retraining therapy: mixing point and total masking are equally effective. Ear and hearing. 2012 Sep-Oct;33(5):588-94.

Studies evaluating neuromodulation interventions other than repetitive transcranial magnetic stimulation

- Ahnblad P, Nordkvist A. A Randomized, Placebo-Controlled, Double-Blind, Parallel Groups Study Evaluating the Performance and Safety of a Steady State Coherent Biomodulator Patch in the Treatment of Subjective Tinnitus. The international tinnitus journal. 2017 Dec 1;21(2):157-67.
- De Ridder D, Vanneste S. EEG driven tDCS versus bifrontal tDCS for tinnitus. Frontiers in Psychiatry. 2012;3(SEP).
- Emmert K, Kopel R, Koush Y, Maire R, Senn P, Van De Ville D, et al. Continuous vs. intermittent neurofeedback to regulate auditory cortex activity of tinnitus patients using real-time fMRI - A pilot study. NeuroImage Clinical. 2017;14:97-104.
- Garin P, Gilain C, Van Damme JP, de Fays K, Jamart J, Ossemann M, et al. Short- and long-lasting tinnitus relief induced by transcranial direct current stimulation. Journal of neurology. 2011 Nov;258(11):1940-8.
- Ghossaini SN, Spitzer JB, Mackins CC, Zschommler A, Diamond BE, Wazen JJ. High-frequency pulsed electromagnetic energy in tinnitus treatment. The Laryngoscope. 2004 Mar;114(3):495-500.
- Hyvarinen P, Makitie A, Aarnisalo AA. Self-Administered Domiciliary tDCS Treatment for Tinnitus: A Double-Blind Sham-Controlled Study. PloS one. 2016;11(4):e0154286.
- Lee SK, Chung H, Chung JH, Yeo SG, Park MS, Byun JY. Effectiveness of transcutaneous electrical stimulation for chronic tinnitus. Acta oto-laryngologica. 2014 Feb;134(2):159-67.
- Li L, Shi H, Wang M. A Pilot Randomized Controlled Trial of Transcutaneous Electrical Nerve Stimulation for Patients With Acute Tinnitus. Medicine. 2019 Jan;98(1):e13793.
- Mielczarek M, Olszewski J. Direct current stimulation of the ear in tinnitus treatment: a double-blind placebo-controlled study. European archives of oto-rhino-laryngology : official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS) : affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery. 2014 Jun;271(6):1815-22.
- Pal N, Maire R, Stephan MA, Herrmann FR, Benninger DH. Transcranial Direct Current Stimulation for the Treatment of Chronic Tinnitus: A Randomized Controlled Study. Brain stimulation. 2015 Nov-Dec;8(6):1101-7.
- Shekhawat GS, Searchfield GD, Stinear CM. Randomized Trial of Transcranial Direct Current Stimulation and Hearing Aids for Tinnitus Management. Neurorehabilitation and neural repair. 2014 Jun;28(5):410-9.

- Shekhawat GS, Vanneste S. High-definition transcranial direct current stimulation of the dorsolateral prefrontal cortex for tinnitus modulation: A preliminary trial. Journal of Neural Transmission. 2018;125(2):163-71.
- Tass PA, Adamchic I, Freund HJ, von Stackelberg T, Hauptmann C. Counteracting tinnitus by acoustic coordinated reset neuromodulation. Restorative neurology and neuroscience. 2012;30(2):137-59.
- Thedinger BS, Karlsen E, Schack SH. Treatment of tinnitus with electrical stimulation: an evaluation of the Audimax Theraband. The Laryngoscope. 1987 Jan;97(1):33-7.
- To WT, Ost J, Hart J, Jr., De Ridder D, Vanneste S. The added value of auditory cortex transcranial random noise stimulation (tRNS) after bifrontal transcranial direct current stimulation (tDCS) for tinnitus. Journal of neural transmission (Vienna, Austria : 1996). 2017 Jan;124(1):79-88.
- Yadollahpour A, Mayo M, Saki N, Rashidi S, Bayat A. A chronic protocol of bilateral transcranial direct current stimulation over auditory cortex for tinnitus treatment: Dataset from a double-blinded randomized controlled trial. F1000Research. 2018;7:733.

Studies evaluating psychological therapies other than cognitive behavioral therapy

- Arif M, Sadlier M, Rajenderkumar D, James J, Tahir T. A randomised controlled study of mindfulness meditation versus relaxation therapy in the management of tinnitus. The Journal of laryngology and otology. 2017 Jun;131(6):501-7.
- Attias J, Shemesh Z, Shoham C, Shahar A, Sohmer H. Efficacy of self-hypnosis for tinnitus relief. Scandinavian audiology. 1990;19(4):245-9.
- Jakes SC, Hallam RS, Rachman S, Hinchcliffe R. The effects of reassurance, relaxation training and distraction on chronic tinnitus sufferers. Behaviour research and therapy. 1986;24(5):497-507.
- Kallogjeri D, Piccirillo JF, Spitznagel E, Jr., Hale S, Nicklaus JE, Hardin FM, et al. Cognitive Training for Adults With Bothersome Tinnitus: A Randomized Clinical Trial. JAMA otolaryngology-- head & neck surgery. 2017 May 1;143(5):443-51.
- Kreuzer PM, Goetz M, Holl M, Schecklmann M, Landgrebe M, Staudinger S, et al. Mindfulness-and body-psychotherapy-based group treatment of chronic tinnitus: a randomized controlled pilot study. BMC complementary and alternative medicine. 2012 Nov 28;12:235.
- McKenna L, Marks EM, Hallsworth CA, Schaette R. Mindfulness-Based Cognitive Therapy as a Treatment for Chronic Tinnitus: A Randomized Controlled Trial. Psychotherapy and psychosomatics. 2017;86(6):351-61.
- Philippot P, Nef F, Clauw L, de Romree M, Segal Z. A randomized controlled trial of mindfulness-based cognitive therapy for treating tinnitus. Clinical psychology & psychotherapy. 2012 Sep;19(5):411-9.

- Podoshin L, Ben-David Y, Fradis M, Gerstel R, Felner H. Idiopathic subjective tinnitus treated by biofeedback, acupuncture and drug therapy. Ear, nose, & throat journal. 1991 May;70(5):284-9.
- Rief W, Weise C, Kley N, Martin A. Psychophysiologic treatment of chronic tinnitus: a randomized clinical trial. Psychosomatic medicine. 2005 Sep-Oct;67(5):833-8.
- Rikkert M, van Rood Y, de Roos C, Ratter J, van den Hout M. A trauma-focused approach for patients with tinnitus: The effectiveness of eye movement desensitization and reprocessing—A multicentre pilot trial. European Journal of Psychotraumatology. 2018;9(1).
- Scott B, Lindberg P, Lyttkens L, Melin L. Psychological treatment of tinnitus. An experimental group study. Scandinavian audiology. 1985;14(4):223-30.
- Weber C, Arck P, Mazurek B, Klapp BF. Impact of a relaxation training on psychometric and immunologic parameters in tinnitus sufferers. Journal of psychosomatic research. 2002 Jan;52(1):29-33.
- White TP, Hoffman SR, Gale EN. Psychophysiological therapy for tinnitus. Ear and hearing. 1986 Dec;7(6):397-9.
- Zarenoe R, Soderlund LL, Andersson G, Ledin T. Motivational Interviewing as an Adjunct to Hearing Rehabilitation for Patients with Tinnitus: A Randomized Controlled Pilot Trial. Journal of the American Academy of Audiology. 2016 Sep;27(8):669-76.

Appendix H. Detailed GRADE Assessments

Table H1. Summary of Findings and Certainty of Evidence (GRADE) for Hearing Aids With Sound-generating Features Compared to Regular Hearing Aids for the Treatment of Tinnitus H-2
Table H2. Summary of Findings and Certainty of Evidence (GRADE) for Altered Auditory Stimulus Interventions Compared to Control Auditory Stimulus for the Treatment of Tinnitus H-3
Table H3. Summary of Findings and Certainty of Evidence (GRADE) for Sound Generators With Information, Education or Counseling Compared to Information, Education, or Counseling Alone for the Treatment of Tinnitus H-4
Table H4. Summary of Findings and Certainty of Evidence (GRADE) for Auditory Attention Training Computer Game Compared to a Control Game for the Treatment of Tinnitus H-5
Table H5. Summary of Findings and Certainty of Evidence (GRADE) for Active Repetitive Transcranial Magnetic Stimulation Compared to Sham Stimulation for the Treatment of Tinnitus H-6
Table H6. Summary of Findings and Certainty of Evidence (GRADE) for Therapist-led Cognitive Behavioral Therapy Interventions Compared to Delayed Treatment or Attention-control for the Treatment of Tinnitus H-8
Table H7. Summary of Findings and Certainty of Evidence (GRADE) for Self-directed (Internet or Book-guided) Cognitive Behavioral Therapy Interventions Compared to Delayed Treatment or Attention-control for the Treatment of Tinnitus H-9
Table H8. Summary of Findings and Certainty of Evidence (GRADE) for Tinnitus-specific Interventions With Sound Therapy Compared to Delayed Treatment or Attention Control for the Treatment of Tinnitus H-10
Table H9. Summary of Findings and Certainty of Evidence (GRADE) for Tinnitus-specific Interventions Without Sound Therapy Compared to Delayed Treatment or Attention-control for the Treatment of Tinnitus H-12

Table H1. Summary of Findings and Certainty of Evidence (GRADE) for Hearing Aids With Sound-generating Features Compared to Regular Hearing Aids for the Treatment of Tinnitus

No. Studies/No. Participants	Summary of Effect	Consistency	Precision	Directness	Study Limitations	Overall Certainty
Tinnitus Distress/Disability						
3 RCTs[16,21,189]/87	No significant differences between groups as measured by the TFI and mini-TQ.	Consistent	Imprecise	Direct	Some	Very low[a,b] No effect
Psychological measures						
None						
Quality of life						
None						
Safety						
None						
Cost						
None						

Notes: [a] Downgraded 2 levels for very serious imprecision; [b] Downgraded 1 level for study limitations.

Abbreviations: RCT = randomized controlled trial; Tinnitus Functional Index; TQ = Tinnitus Questionnaire.

Table H2. Summary of Findings and Certainty of Evidence (GRADE) for Altered Auditory Stimulus Interventions Compared to Control Auditory Stimulus for the Treatment of Tinnitus

No. Studies/No. Participants	Summary of Effect	Consistency	Precision	Directness	Study Limitations	Overall Certainty / Direction of Effect
Tinnitus Distress/Disability						
4 RCTs[15,17,20,22]/219	Mixed findings: 1 study reported a significant difference (favoring intervention) with the THI[a] and 1 study reported significant difference with VAS loudness; no significant differences were observed in between groups in the other 2 studies as measured by VAS loudness, THQ, VAS total score, and TFI.	Inconsistent	Imprecise	Direct	Some	Very low[b,c] Unable to determine
Psychological measures						
1 RCT[17]/50	No significant difference in HADS-A at 1 year; no significant difference in HADS-D at 6 months or 1 year. Larger reduction in HADS-A at 6 months (2.7 points).	NA	Imprecise	Direct	Some	Very low[b,c] No effect
Quality of life						
None						
Safety						
1 RCT[20]/100	No statistically significant difference in incidence of adverse events defined by study authors (additional sounds, awareness of tinnitus, psychological stress, bodily changes); notched music training (24%) vs. placebo music (30%).	NA	Imprecise	Direct	Some	Very low[b,c] No effect
Cost						
None						

Notes: [a] This study also measured outcomes using the TFI and found no significant difference with the TFI. [b] Downgraded 2 levels for very serious imprecision; [c] Downgraded 1 level for study limitations.

Abbreviations: HADS = Hospital Anxiety and Depression scale; NA = not applicable, single study body of evidence; RCT = randomized controlled trial; THQ = Tinnitus Handicap Questionnaire; Tinnitus Functional Index; TQ = Tinnitus Questionnaire; VAS = visual analog scale.

Table H3. Summary of Findings and Certainty of Evidence (GRADE) for Sound Generators With Information, Education or Counseling Compared to Information, Education, or Counseling Alone for the Treatment of Tinnitus

No. Studies/No. Participants	Summary of Effect	Consistency	Precision	Directness	Study Limitations	Overall Certainty
Tinnitus Distress/Disability						
3 RCTs[19,23,24]/234	No statistically significant differences favoring sound-generating interventions as measured by TRQ, TQ, VAS loudness, and other VAS assessments.	Consistent	Imprecise	Direct	Some	Very low[a,b] No effect
Psychological measures						
1 RCT[19]/48	No statistically significant differences in coping or stress as measured by WCCL-R and DSP.	NA	Imprecise	Direct	Some	Very low[a,b] Unable to determine
Quality of life						
None						
Safety						
None						
Cost						
None						

Notes: [a] Downgraded 2 levels for very serious imprecision; [b] Downgraded 1 level for study limitations.

Abbreviations: DSP = Derogatis Stress Profile; NA = not applicable, single study body of evidence; RCT = randomized controlled trial; TQ = Tinnitus Questionnaire; TRQ = Tinnitus Reaction Questionnaire; VAS = visual analog scale; WCCL-R = Ways of Coping Checklist Revised.

Table H4. Summary of Findings and Certainty of Evidence (GRADE) for Auditory Attention Training Computer Game Compared to a Control Game for the Treatment of Tinnitus

No. Studies/No. Participants	Summary of Effect	Consistency	Precision	Directness	Study Limitations	Overall Certainty
Tinnitus Distress/Disability						
1 RCTs[18] /31	No statistically significant differences as measured by the THI, TFI, and TSS.	NA	Imprecise	Direct	Some	Very low[a,b] Unable to determine
Psychological measures						
None						
Quality of life						
None						
Safety						
None						
Cost						
None						

Notes: [a] Downgraded 2 levels for very serious imprecision; [b] Downgraded 1 level for study limitations.

Abbreviations: NA = not applicable, single study body of evidence; RCT = randomized controlled trial; THI = Tinnitus Handicap Inventory; TFI = Tinnitus Functional Index; TSS = Tinnitus Severity Scale.

Table H5. Summary of Findings and Certainty of Evidence (GRADE) for Active Repetitive Transcranial Magnetic Stimulation Compared to Sham Stimulation for the Treatment of Tinnitus

No. Studies/No. Participants	Summary of Effect	Consistency	Precision	Directness	Study Limitations	Overall Certainty/ Direction
Tinnitus distress/disability immediately after treatment up to 6 months						
18 RCTs[26-28,30-36,38-42]/760	Various measures reported (Tinnitus Handicap Inventory, Tinnitus Questionnaire, Visual Analog Scales of loudness, discomfort, annoyance, distress, Tinnitus Handicap Questionnaire, Tinnitus Reaction Questionnaire, Tinnitus Functional Index, and global measures of improvement; many were primary study outcomes. No differences between active rTMS and sham rTMS for nearly all comparisons; 2 studies reported statistically significant differences favoring active rTMS immediately after treatment but these differences were not durable at subsequent follow-up timepoints.	Mostly consistent	Imprecise	Direct	Some	Low[a, b] No effect
Psychological measures immediately after treatment up to 6 months						
5 RCTs[30,32,34,39,41]/247	No significant differences in measures of depression (Beck Depression Inventory, Hamilton Depression Scale), anxiety (Hamilton Anxiety Scale), or sleep (Jenkins Sleep Evaluation Questionnaire) between active rTMS and sham rTMS. Not primary study outcomes in any study.	Consistent	Imprecise	Direct	Some	Very low[b,c] No effect
Quality of life at 6 months (SF-12 Physical Health Component and Mental Health Component Score)						
1 RCT[32]/153	No significant difference between active and sham rTMS; not a primary study outcome.	NA	Imprecise	Direct	Some	Very low[b,c] No effect
Safety (adverse events, serious adverse events, side effects during treatment and over various lengths of followup)						
14 RCTs[26,28-34,36-41]/526	Mixed findings; 5 studies reported no adverse events in either group, 3 studies reported a similar incidence of adverse or serious adverse events for participants allocated to active rTMS compared to sham rTMS, 2 studies reported a higher incidence of events in participants allocated to active rTMS compared to sham rTMS, and 1 study reported a higher incidence in participants allocated to sham rTMS compared to active rTMS. Three studies did not report events by group but reported no major or sustained effects. Not primary study outcome in any study.	Inconsistent	Imprecise	Direct	Some	Very low[b,c] Unable to determine
Cost						
None						

Notes: [a] Downgraded 1 level for imprecision; [b] Downgraded 1 level for study limitations; [c] Downgraded 2 levels for very serious imprecision.

Abbreviations: NA = not applicable, single study body of evidence; RCT = randomized controlled trial; rTMS = repetitive transcranial magnetic stimulation.

Table H6. Summary of Findings and Certainty of Evidence (GRADE) for Therapist-led Cognitive Behavioral Therapy Interventions Compared to Delayed Treatment or Attention-control for the Treatment of Tinnitus

No. Studies/No. Participants	Summary of Effect	Consistency	Precision	Directness	Study Limitations	Overall Certainty/ Direction
Tinnitus distress/disability						
13 RCTs[45,47,49,50,53,54,56-59,62,63,65] / 1,743	Primary study aim in 3 studies. Effect estimates usually favored larger improvements in the interventions groups as assessed by various measures of tinnitus distress and disability; however, findings were not statistically significant in all studies.	Mostly Consistent	Imprecise	Direct	Some	Low[a,b] for benefit
Psychological measures						
11 RCTs[45,49,50,53,54,56,57,59,61-63] / 1,100	Not a primary study aim in any study. While effect estimates usually favored larger improvements in the intervention groups on measures of depression, anxiety, general well-being, impact on sleep, and coping, results were only statistically significant in some studies.	Mostly Consistent	Imprecise	Direct	Some	Low[a,b] for benefit
Quality of life						
None						
Safety						
3 RCTs[54,61,65] / 436	Adverse events rare to none.	Consistent	Imprecise	Direct	Some	Very low[b, c] for no harm
Cost						
None						

Notes: [a] Downgraded 1 level for imprecision; [b] Downgraded 1 level for study limitations; [c] Downgraded 2 levels for very serious imprecision.

Abbreviations: RCT = randomized controlled trial.

Table H7. Summary of Findings and Certainty of Evidence (GRADE) for Self-directed (Internet or Book-guided) Cognitive Behavioral Therapy Interventions Compared to Delayed Treatment or Attention-control for the Treatment of Tinnitus

No. Studies/No. Participants	Summary of Effect	Consistency	Precision	Directness	Study Limitations	Overall Certainty / Direction
Tinnitus distress/disability						
9 RCTs[46,48-52,55,60,64] / 946	Primary study aim in 7 studies. Effect estimates usually favored larger improvements in the interventions groups as assessed by various measures of tinnitus distress and disability; however, findings were not statistically significant in all studies.	Mostly Consistent	Imprecise	Direct	Some	Low[a,b] for benefit
Psychological measures						
8 RCTs[46,48-51,55,60,64] / 784	Not a primary study aim in any study. While effect estimates usually favored larger improvements in the intervention groups on measures of depression, anxiety, stress, and impact on sleep; results were only statistically significant in some studies of depression, anxiety, and sleep.	Mostly Consistent	Imprecise	Direct	Some	Low[a,b] for benefit
Quality of life						
2 RCTs[51,64] / 120	Not a primary study aim in any study. Larger numeric improvement for treatment group (effect size 0.45) in 1 study but not statistically significant. No significant differences in the other study, effect size NR.	Mostly Consistent	Imprecise	Direct	Some	Very low[b,c] No effect
Safety						
None						
Cost						
None						

Notes: [a] Downgraded 1 level for imprecision; [b] Downgraded 1 level for study limitations; [c] Downgraded 2 levels for very serious imprecision.

Abbreviations: NR = not reported; RCT = randomized controlled trial.

Table H8. Summary of Findings and Certainty of Evidence (GRADE) for Tinnitus-specific Interventions With Sound Therapy Compared to Delayed Treatment or Attention Control for the Treatment of Tinnitus

No. Studies/No. Participants	Summary of Effect	Consistency	Precision	Directness	Study Limitations	Overall Certainty
Tinnitus distress/disability						
7 RCTs[24,58,67-69,72,73]/937	All but 1 study observed statistically larger improvements with the intervention as measured by THI, TQ, TRQ, and VAS assessments at most, but not all timepoints.	Mostly consistent	Imprecise	Direct	Some	Low[a,b] for benefit
Psychological measures						
2 RCTs[68,69]/556	Mixed findings between studies; the study with the longer duration (8 months) demonstrated statistically significant larger improvements on depression as measured by HADS-D for the intervention compared to the usual care control at 8 and 12 months but not at 3 months; the study with the shorter duration (10 weeks) observed no significant differences on measures of depression (HADS-D), anxiety (HADS-A) or sleep (ISI).	Inconsistent	Imprecise	Direct	Some	Very low[a,b,d] Relationship cannot be determined
Quality of life						
2 RCTs[68,69]/556	Mixed findings between studies; the study with the longer duration (8 months) demonstrated statistically significant larger improvements on QoL for the intervention compared to the usual care control at 8 and 12 months but not at 3 months; the study with the shorter duration (10 weeks) observed no significant differences as measured by the QoLI.	Inconsistent	Imprecise	Direct	Some	Very low[a,b,d] Relationship cannot be determined
Safety						
1 RCT[68]/492	No adverse events reported.	NA	Imprecise	Direct	Some	Very low[b,c] Relationship cannot be determined
Cost						
1 RCT[68]/492	Cost per QALY gained $10,456 (95% CI, NR) from healthcare payor perspective and $24,580 (95% CI, NR) from societal perspective.	NA	Imprecise	Direct	Some	Very low[b,c] Relationship cannot be determined

Notes: [a] Downgraded 1 level for imprecision; [b] Downgraded 1 level for study limitations; [c] Downgraded 2 levels for very serious imprecision. [d] Downgraded 1 level for inconsistency.

Abbreviations: CI = confidence interval; HADS-A and HADS-D = Hospital Anxiety and Depression Scale; ISI = Insomnia Severity Index; NA = not applicable, single study body of evidence; NR = not reported; QALY = quality adjusted life year; QoLI = Quality of Life Inventory; RCT = randomized controlled trial; THI = Tinnitus Handicap Inventory; TQ = Tinnitus Questionnaire; TRQ = Tinnitus Reaction Questionnaire; VAS = visual analog scale.

Table H9. Summary of Findings and Certainty of Evidence (GRADE) for Tinnitus-specific Interventions Without Sound Therapy Compared to Delayed Treatment or Attention-control for the Treatment of Tinnitus

No. Studies/No. Participants	Summary of Effect	Consistency	Precision	Directness	Study Limitations	Overall Certainty
Tinnitus distress/disability						
3 RCTs[70,71,74]/409	Larger improvements with the intervention as measured by TQ and TSI. However, 1 study only found statistically significant improvements when compared to a no treatment control; findings versus an attention control group were attenuated and only significant at 12 months, but not 6 months.	Inconsistent	Imprecise	Direct	Some	Very low[a, b, c] for benefit
Psychological measures						
1 RCT[70]/90	Statistically significant larger improvements for depression as measured by the ADS; no differences on level of stress as reported by the PSS.	NA	Imprecise	Direct	Some	Very low[b, c, d] Relationship cannot be determined
Quality of life						
None						
Safety						
None						
Cost						
None						

Notes: [a] Downgraded 1 level for imprecision; [b] Downgraded 1 level for study limitations; [c] Downgraded 1 level for inconsistency; [d] Downgraded 2 levels for very serious imprecision.

Abbreviations: ADS = Allegmeine Depression Scale; NA = not applicable, single study body of evidence; NR = not reported; PSS = perceived stress scale; TQ = Tinnitus Questionnaire; TSI = Tinnitus Severity Index.

Appendix I. Agree-II Clinical Practice Guideline Ratings

Table I1. AGREE-II Ratings for Clinical Practice Guidelines-Part 1 ..... I-2
Table I2. AGREE-II Ratings for Clinical Practice Guidelines-Part 2 ..... I-3
Table I3. AGREE-II Ratings for Clinical Practice Guidelines-Part 3 ..... I-4
Table I4. AGREE-II Ratings for Clinical Practice Guidelines-Part 4 ..... I-5

Table I1. AGREE-II Ratings for Clinical Practice Guidelines-Part 1

Guideline Title, Year	Domain 1: SCOPE AND PURPOSE			Domain 2: STAKEHOLDER INVOLVEMENT		
	The overall objectives of the guideline are described.	The health questions covered by the guideline is (are) specifically described.	The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	The guideline development group includes individuals from all relevant professional groups.	The views and preferences of the target population (patients, public, etc.) have been sought.	The target users of the guideline are clearly defined.
A multidisciplinary European guideline for tinnitus: diagnostics, assessment, and treatment, 2019 [86]	7	7	7	7	3	7
VA/DoD Clinical Practice Guidelines: Management of Concussion-mild Traumatic Brain Injury (mTBI), 2016[85]	7	7	7	5	3	7
Association of the Scientific Medical Societies in Germany Guideline 01 7/064: Chronic Tinnitus, 2015[87]	6	6	6	7	7	7
International Federation of Clinical Neurophysiology: Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation, 2014[79]	5	6	6	4	3	4
American Academy of Otolaryngology-Head and Neck Surgery Clinical Practice Guideline: Tinnitus, 2014[88]	7	7	7	7	6	7

Table I2. AGREE-II Ratings for Clinical Practice Guidelines-Part 2

Title, Year	Domain 3: RIGOR OF DEVELOPMENT							
	Systematic methods were used to search for evidence.	The criteria for selecting the evidence are clearly described.	The strengths and limitations of the body of evidence are clearly described.	The methods for formulating the recommendations are clearly described.	The health benefits, side effects, and risks have been considered in formulating the recommendations.	There is an explicit link between the recommendations and the supporting evidence.	The guideline has been externally reviewed by experts prior to its publication.	A procedure for updating the guideline is provided.
A multidisciplinary European guideline for tinnitus: diagnostics, assessment, and treatment, 2019 [86,208]	5	7	4	6	6	6	7	4
VA/DoD Clinical Practice Guidelines: Management of Concussion-mild Traumatic Brain Injury (mTBI), 2016[85]	7	4	4	7	6	5	7	6
Association of the Scientific Medical Societies in Germany Guideline 017/064: Chronic Tinnitus, 2015[87]	3	5	4	5	6	6	6	7
Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation, 2014[79]	3	4	4	3	6	6	4	3
American Academy of Otolaryngology-Head and Neck Surgery Clinical Practice Guidelines: Tinnitus, 2014[88]	6	4	4	6	6	4	6	4

Table I3. AGREE-II Ratings for Clinical Practice Guidelines-Part 3

	Domain 4: CLARITY OF PRESENTATION			Domain 5: APPLICABILITY			
Title, Year	**The recommendations are specific and unambiguous.**	**The different options for management of the condition or health issue are clearly presented.**	**Key recommend-ations are easily identifiable.**	**The guideline describes facilitators and barriers to its application.**	**The guideline provides advice and/or tools on how the recommendations can be put into practice.**	**The potential resource implications of applying the recommendations have been considered.**	**The guideline presents monitoring and/or auditing criteria.**
A multidisciplinary European guideline for tinnitus: diagnostics, assessment, and treatment, 2019 [86]	6	6	7	6	7	6	5
VA/DoD Clinical Practice Guidelines: Management of Concussion-mild Traumatic Brain Injury (mTBI), 2016[85]	3	3	5	4	5	3	4
Association of the Scientific Medical Societies in Germany Guideline 01 7/064: Chronic Tinnitus, 2015[87]	5	6	5	4	5	4	4
Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation, 2014[79]	3	6	5	6	5	5	4
American Academy of Otolaryngology-Head and Neck Surgery Clinical Practice Guidelines: Tinnitus, 2014[88]	6	6	7	5	6	6	4

Table I4. AGREE-II Ratings for Clinical Practice Guidelines-Part 4

Title, Year	Domain 6: EDITORIAL INDEPENDENCE		OVERALL ASSESSMENT
	The views of the funding body have not influenced the content of the guideline	Competing interests of guideline development group members have been recorded and addressed.	Rate the overall quality of this guideline.
A multidisciplinary European guideline for tinnitus: diagnostics, assessment, and treatment, 2019 [86]	5	5	6
VA/DoD Clinical Practice Guidelines: Management of Concussion-mild Traumatic Brain Injury (mTBI), 2016[85]	5	6	5
Association of the Scientific Medical Societies in Germany Guideline 01 7/064: Chronic Tinnitus, 2015[87]	5	7	5
Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation, 2014[79]	5	7	4
American Academy of Otolaryngology-Head and Neck Surgery Clinical Practice Guidelines: Tinnitus, 2014[88]	5	6	5

Appendix J. Additional Information About Ongoing Studies

Table J1. Relevant Ongoing Clinical Trials by Estimated Primary Completion Date

Record Number	Status	Estimated Primary Completion Date	Title	Intervention Category
NCT03621735	Enrolling by invitation	January 2019	Reversing Synchronized Brain Circuits With Targeted Auditory-Somatosensory Stimulation to Treat Phantom Percepts	Neuromodulation
NCT03773926	Recruiting	January 2019	Neurofeedback Therapy for Treating Tinnitus	Neuromodulation
NCT04026932	Not yet recruiting	February 2019	The Clinical Effects of Modified TRS Treatment	Sound Therapies
NCT03657615	Recruiting	June 2019	Hearing Aid Impact on Chronic Tinnitus Patients Evaluated by Resting State PET.	Sound Therapies
NCT02669069	Active, not recruiting	July 2019	Treatment Evaluation of Neuromodulation for Tinnitus (TENT-A)	Neuromodulation
NCT03544359	Recruiting	August 2019	MRI Study of Noninvasive Transcranial Electrical Stimulation in Tinnitus	Neuromodulation
NCT03888521	Active, not recruiting	September 2019	Evaluating the GN ReSound Relief App Using task-and Rest-based fMRI	Sound Therapies
NCT00926237	Recruiting	September 2019	Effect of rTMS on Resting State Brain Activity in Tinnitus	Neuromodulation
NCT02617953	Enrolling by invitation	September 2019	Objective Diagnosis Method and Efficacy of Repetitive Transcranial Magnetic Stimulation as a Treatment for Tinnitus	Neuromodulation
NCT03530306	Active, not recruiting	September 2019	Treatment Evaluation of Neuromodulation for Tinnitus—Stage A2	Neuromodulation
NCT03309696	Recruiting	October 2019	Regulating Homeostatic Plasticity and the Physiological Response to rTMS	Neuromodulation
NCT02774122	Active, not recruiting	October 2019	Cochlear Alternating Acoustic Beam Therapy (CAABT) Versus Masking Intervention for Tinnitus	≥2 Therapies
NCT01886092	Enrolling by invitation	October 2019	Repetitive Transcranial Magnetic Stimulation as a Treatment for Tinnitus	Neuromodulation
NCT03688113	Not yet enrolling	December 2019	Tinnitus Treatment Using a Smartphone Application	Sound Therapies
NCT02615600	Recruiting	December 2019	Daily Bitemporal Low-frequency Transcranial Random Noise Stimulation in Tinnitus (tRNS2-tin)	Neuromodulation
NCT03699826	Enrolling by invitation	December 2019	Experimental Tinnitus Treatment With Transcranial Magnetic Stimulation	Neuromodulation
NCT03759834	Active, not recruiting	December 2019	Cochlear Promontory Stimulation for Treatment of Tinnitus	Neuromodulation
NCT03114878	Recruiting	December 2019	The Value of EMDR in the Treatment of Tinnitus	≥2 Therapies
NCT03022084	Active, not recruiting	December 2019	Clinical Trial of Sound-Based Versus Behavioral Therapy for Tinnitus	Psychological and Behavioral Therapies
NCT03764826	Recruiting	December 2019	Study on the Effect of Sound Therapy on Chronic Primary Tinnitus	≥2 Therapies

Record Number	Status	Estimated Primary Completion Date	Title	Intervention Category
NCT02071732	Recruiting	December 2019	Therapeutic Effect of Repetitive Transcranial Magnetic Stimulation on Tinnitus	Neuromodulation
NCT03386123	Active, not recruiting	December 2019	A Comparison of CBTi and Usual Treatment for Tinnitus-Related Insomnia	Psychological and Behavioral Therapies
NCT03716544	Recruiting	December 2019	Efficacy of Amplification With Hearing Aids for Tinnitus Relief	Sound Therapies
NCT03143842	Active, not recruiting	January 2020	Investigating Accelerated Learning in Tinnitus Participants Implanted With Vagus Nerve Stimulation	Neuromodulation
NCT03957122	Recruiting	March 2020	Individualized Treatment of Patients With Chronic Tinnitus With Repetitive Transcranial Magnetic Stimulation	Neuromodulation
NCT03702166	Recruiting	June 2020	Network Dysregulation Among Individuals With Comorbid Tinnitus and PTSD	Psychological and Behavioral Therapies
NCT03550430	Recruiting	July 2020	Neurofeedback for Tinnitus—Does Frequency Specificity Matter?	Neuromodulation
NCT03895047	Recruiting	August 2020	ICCAC-ToNF & Tinnitus	Neuromodulation
NCT03511807	Recruiting	January 2021	Acoustic and Electrical Stimulation for the Treatment of Tinnitus	≥2 Therapies
NCT03904264	Not yet recruiting	July 2021	Feasibility and Acceptability of Using Low-Gain Hearing Aids for Bothersome Tinnitus	Sound Therapies
NCT04004260	Not yet recruiting	August 2021	CBT-based Internet Intervention for Adults With Tinnitus in the United States	Psychological and Behavioral Therapies
NCT03754127	Recruiting	September 2022	A Randomized Controlled HD-tDCS Trial: Effects on Tinnitus Severity and Cognition	Neuromodulation
NCT03429777	Not yet recruiting	May 2024	Validation of a Smartphone-Based Hearing-in-Noise Test (HearMe)	Sound Therapies

Abbreviations: CBT(i) = Cognitive Behavioral Therapy (for insomnia); EMDR = Eye Movement Desensitization and Reprocessing; fMRI = Functional Magnetic Resonance Imaging; HD-tDCS = High Definition-Transcranial Direct Current Stimulation; ICCAC-ToNF = Insula Dorsal Anterior Cingulate Cortez & Auditory Cortex-Tomographical Neurofeedback Training; NCT = National Clinical Trial; PET = Positron Emission Tomography; PTSD = Post-traumatic stress disorder; rTMS = Repetitive Transcranial Magnetic Stimulation; TRS = Tinnitus Relieving Sound.